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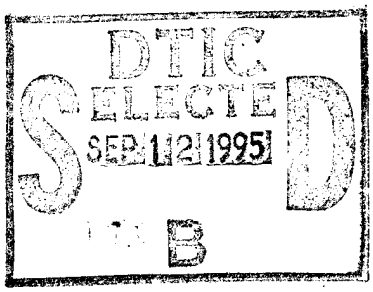
Sustaining Female UH-60 Helicopter Performance with Dexedrine during Sustained Operations: A Simulator Study



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The efficacy of Dexedrine for sustaining the performance of six female UH-60 pilots under conditions of moderate sleep deprivation was determined. Each subject was exposed to one week of testing which included 2, 40-hour sleep deprivation periods. During both deprivation periods, there were 5 equally-spaced test sessions, each of which included a UH-60 simulator flight, an electroencephalographic (EEG) evaluation, a test on the Microsoft Flight Simulator, a Profile of Mood States questionnaire, and a cognitive evaluation on the Synthetic Work Battery. These testing sessions began at 0100, 0500, 0900, 1300, and 1700. During one of the deprivation periods, subjects were administered a 10-mg dose of Dexedrine one hour prior to each of the first three sessions (for a total of 30 mgs). During the other deprivation period, subjects were administered placebos. A double-blind administration scheme was used. Vital signs were monitored at regular intervals throughout the study.

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The results indicated that Dexedrine improved at least one aspect of pilot performance on all but two of the nine maneuvers flown (there were no differences on the hovers or hovering turns). In the majority of cases where there were significant interactions between drug and time-of-day, the largest differences between Dexedrine and placebo were observed at 0900. Electroencephalographic data showed that alertness was generally decreased under the placebo condition--there was more delta and theta activity under placebo than under Dexedrine. The scores from the POMS revealed that subjects felt more alert under Dexedrine than placebo, especially during the morning sessions (although subjects reported feeling more vigorous under Dexedrine at 1540 as well). The results from the synthetic work battery suggested there were few effects on this cognitive test. Vital signs data showed that Dexedrine increased both pulse and blood pressure, although the observed elevations were not clinically significant. Polysomnographic findings indicated that sleep quality was adversely impacted by Dexedrine, but not to a great extent. In fact, subjects generally slept better on both the Dexedrine and placebo recovery nights than they did on the baseline night (presumably because of the pressure to sleep from sleep deprivation).

Overall, it appears that Dexedrine effectively sustained the performance and mood of female UH-60 pilots despite short-term sleep loss. There were no adverse behavioral or physiological side effects.

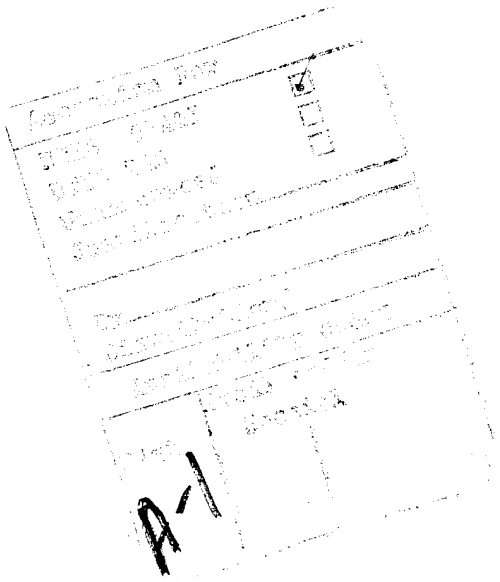


Table of contents

Table of contents (continued)

Introduction

Current military doctrine requires that Army aviation units operate around the clock during times of conflict because the success of battlefield operations depends on maintaining the momentum of continuous day-night operations (Department of the Army, 1989). In part, due to the significant improvement in night fighting capability offered by night vision devices, night helicopter operations now constitute a substantial component of the modern aviation mission. Combining efficient day and night fighting capabilities across successive 24-hour periods places a significant strain on enemy resources and presents a clear tactical advantage for U.S. forces.

However, there are difficulties inherent in maintaining effective round-the-clock operations. Although aircraft can function for extended periods without adverse effects, human operators need periodic sleep for the restitution of both body and brain (Horne, 1978). Depriving humans of proper restorative sleep produces attentional lapses and slower reaction times which are associated with poor performance (Krueger, 1989).

Because it is virtually impossible for aviation crews to receive adequate sleep and rest during combat operations, it is essential that the military explore countermeasures to offset the performance decrements associated with sleep debt. Given that personnel resources are dwindling while mission demands are expanding, pharmacological countermeasures (i.e., stimulants) may be the only viable alternative in some situations. In addition, there is a need to understand the full impact of stimulant medications in both male and female personnel since female pilots recently have been authorized to fly combat missions.

Background

General

A variety of different strategies have been investigated to minimize fatigue-related performance decrements in various work settings (Babkoff and Krueger, 1992), but the combat situation remains problematic because it is intense and unpredictable. As Cornum (1994) has pointed out, while it is desirable to control the timing and duration of sleep periods via sleep management programs, this approach often is not feasible in the operational setting. One illustration of this fact was offered by recent

research which suggested that despite commanders' best efforts to properly manage crew rest in the combat environment, sleep deprivation was a problem for several Army pilots during Desert Storm even though the combat period was short (Caldwell, 1992). In addition, it has been reported that Air Force F-15C pilots suffered significant fatigue and circadian disruptions when flying combat air patrol missions over Iraq (Cornum, 1994).

When operational constraints prevent the use of behavioral strategies for the alleviation of aircrew fatigue, pharmacological countermeasures (stimulants) may be the only option for maintaining aviator performance. Of the pharmacological compounds available, it has been suggested that amphetamines offer the greatest potential for counteracting performance decrements attributable to sustained operations (Shappell, Neri, and DeJohn, 1992). Since dextroamphetamine is the most potent of the amphetamines (Smith and Davis, 1977), Dexedrine has been the stimulant of choice in several studies and in the operational environment.

Dexedrine®

Dexedrine® (Smith, Kline, and French) is dextroamphetamine sulfate, supplied in 5, 10, and 15 mg Spansule sustained-release capsules, 5 mg tablets, and an elixir supplying 5 mg amphetamine per 5 ml (Physicians' Desk Reference, 1993). Dexedrine can be expected to exert a variety of typical amphetamine effects both on the central and peripheral nervous system (Weiner, 1980).

Oral amphetamine elevates blood pressure (systolic and diastolic), and sometimes increases heart rate. The bronchial muscle is relaxed slightly, but respiration rate and volume are unaffected. The urinary bladder sphincter is constricted. Gastrointestinal effects are not predictable. The CNS is stimulated, and the depressant effects of other drugs are reduced. Psychological effects of doses ranging from 5-30 mg include increased wakefulness, alertness, initiative, and concentration, with elevated mood, sometimes euphoria, improved task performance, and decreased fatigue. Amphetamines have been used to prolong performance of vigilance tasks, and in situations where performance has degraded due to sleep loss, amphetamines have produced improvements in tasks requiring sustained attention. Amphetamines alter sleep EEG by cutting in half the typical amount of REM sleep. They alter the waking EEG by increasing desynchronous activity and producing a shift toward higher frequencies. Amphetamine suppresses the appetite.

Occasionally, amphetamine will produce a slight elevation in body temperature (Weiner, 1980).

Dosage

The usual chronic oral dose of dextroamphetamine is 5 mg, 2-3 times daily; however, studies employing the drug to prolong wakefulness and performance typically employ larger doses in the range of 10-20 mg (Weiss and Laties, 1967). Prior to administering normal therapeutic doses to humans, a test dose of 2.5 mg is recommended since toxic manifestations have been seen (as an idiosyncracy) after even a 2-mg dose, although reactions are rare with doses under 15 mg (Weiner, 1980).

Pharmacokinetics

A single dose of two 5 mg tablets has been shown to produce an average peak blood level of 29.2 ng/ml at approximately 2 hours. The average half life is 10.25 hours (Physicians' Desk Reference, 1993).

Gender differences

While there have been no studies of gender differences relative to Dexedrine's effects, the pharmacology literature contains numerous general references to real or suspected gender variations in drug absorption, distribution, metabolism and excretion. Yonkers et al. (1992) reviewed the role of gender in the pharmacokinetics and pharmacodynamics of psychotropic medication.

Drug absorption may be affected by factors such as higher gastric pH in females, or by a prolonged transit time during the luteal phase of the menstrual cycle. Further, women tend to empty both solids and liquids more slowly from the GI tract. However, the literature is conflicting, and these effects, if present, may counteract each other. For example, a slower gastric emptying rate would decrease the amount of drug absorbed, while prolonged transit time in the GI tract would have the opposite effect.

Differences in vascular and tissue volume in females can affect drug distribution, while drugs with a high affinity for adipose tissue should have a greater volume of distribution in

females (Yonkers et al., 1992). Drug metabolism can be affected by differences in hepatic microsomal enzyme activity, although these enzymes are also affected by smoking and menstrual cycle changes. Both male-specific and female-specific versions of Cytochrome P-450 have been identified. Differences in the biotransformation of nicotine, aspirin, and heparin have been reported in humans (Sipes and Gandolfi, 1986).

The menstrual cycle also may have varying effects on the activity of a drug (Yonkers et al., 1992). Women who experience significant water retention may have different volumes of distribution at different points in the menstrual cycle; however, the practical significance of this factor has not yet been determined for most pharmacological compounds.

Exogenous ovarian hormones also can affect the metabolism of medications by inducing changes in hepatic microsomal enzyme activity. For example, females taking oral contraceptives and the hypnotic diazepam can display more CNS effects during menses (Ellinwood et al., 1983).

Generally, there is reason to suspect different drug kinetics and effects in females compared to males. Dexedrine, although safe and effective in males, could produce surprising effects if administered to females in the operational setting. However, from the available literature, it is impossible to determine whether females will be more or less sensitive, and also it is difficult to estimate whether there will be differences in half-life, etc. Unfortunately, there have been no systematic studies of gender differences in responsiveness to Dexedrine.

Aviator performance effects of amphetamine

Numerous investigations have proven that amphetamines are effective for enhancing physical performance, vigilance, alertness, cognition, and military performance (see Caldwell et al., 1994), but there have been very few aviation-related studies. However, the few studies which exist support the contention that amphetamines are effective countermeasures for sleep loss and fatigue in aviation personnel.

Pascoe, Nicholson, and Turner (1994) have suggested that sometimes, even in situations where aviators do receive enough sleep, they may require pharmacological assistance to maintain

appropriate levels of alertness required in fatiguing continuous combat operations.

Senechal (1988) reported that EF-111A Raven jet crews who were administered 5 mg Dexedrine during an Air Force strike on Libya in April of 1986 experienced positive effects in terms of overcoming the fatigue of the mission itself and the sleep deprivation which occurred during earlier preparation for the mission. There were no in-flight or landing problems, and all of these electronic-jamming aircraft returned safely to base.

Cornum (1994) reported that dextroamphetamine also was used with 35 F-15C pilots who were flying combat air patrol missions during Operation Desert Shield/Storm. These pilots were not only flying long missions (6-11 hours), but they were sleep deprived and suffering from circadian desynchronosis as well. To counteract potentially lethal performance decrements, the pilots were issued 5-6 dextroamphetamine tablets (5 mg) at the beginning of flights and were told to self-administer one tablet every 2-4 hours as needed to maintain alertness until landing. Aviators who used the drug reported clear benefit, and the unit commander ultimately concluded that dextroamphetamine administration contributed significantly to the safety of operations. There were no reported adverse effects, even in personnel who took 10 mg at a time, and no aviators reported a need to continue the drug once proper work/sleep schedules were reinstated.

Emonson and Vanderbeek (1995) indicated that 65 percent of the Air Force pilots who were surveyed used amphetamines occasionally during Operation Desert Storm to reduce aircrew fatigue. Approximately 60 percent of the pilots who used amphetamines thought they were beneficial. Dextroamphetamine taken in 5-mg doses every 4 hours reduced cockpit fatigue and enhanced safety without producing side effects.

These anecdotal reports recently have been supported in a controlled laboratory investigation of the effects of Dexedrine on sleep deprived male aviators. Caldwell, Caldwell, Crowley, and Jones (in press) conducted a placebo-controlled study of 6 Army helicopter pilots who completed UH-60 simulator flights, psychological evaluations, and electrophysiological assessments throughout 40-hour sleep deprivation periods. Simulator flights occurred at 0100, 0500, 0900, 1300, and 1700. One hour prior to each of the first 3 flights, the aviators were given 10 mg of Dexedrine or placebo. Analyses of the flight maneuvers revealed that Dexedrine improved aviator control on the majority of maneuvers including the descents, straight-and-levels, standard-

rate turns, stationary hovers, low-level navigation, and a left-descending turn. Performance was not enhanced on hovering turns or formation flight. The times of day at which Dexedrine most noticeably facilitated flight performance were 0500, 0900, and 1700 (after 22, 26, and 34 hours of continuous wakefulness). EEG and mood data showed that general alertness also was sustained significantly by Dexedrine. Although the quality of recovery sleep after Dexedrine was compromised somewhat, there were no clinically significant behavioral or physiological effects in any of the subjects.

Thus, it appears that Dexedrine is a safe and effective means for sustaining performance during short periods of sleep loss in male helicopter pilots. However, there has been no research conducted on the efficacy of Dexedrine for maintaining alertness in female pilots. Since recent shifts in U.S. Army policy have opened front-line combat positions to female soldiers, it is essential to replicate the earlier findings regarding the effectiveness of Dexedrine in male aviators with a similar study on a sample of female aviators. In future combat scenarios, females undoubtedly will find themselves in situations where stimulant drug therapy is an option. Because of the possibility of differences in drug metabolism between males and females, it is important to show that operationally critical drugs (such as Dexedrine) are as safe and effective in women, as they are in men.

Objectives

This investigation was conducted to determine the effects of dextroamphetamine (Dexedrine) for safely sustaining alertness and performance of female helicopter pilots despite sleep loss in an aviation context. The study employed a variety of assessments to determine the effects of repeated 10-mg doses of Dexedrine on: 1) flight performance measured in a UH-60 simulator, 2) CNS function measured by EEG assessments, 3) psychomotor skill measured by a desktop flight simulator, 4) mood measured by the Profile of Mood States, 5) vigilance measured by the Synthetic Work Battery, 6) sleep architecture measured by polysomnography, and 7) vital signs (pulse and blood pressure).

Methods

Subjects

Six UH-60 qualified, female aviators (between the ages of 24 and 35 years, with a mean age of 29.5 years) participated in this investigation after signing appropriate consent forms and passing a medical evaluation. Subjects were not permitted to consume caffeinated beverages, fruit, fruit juice (with the exception of orange juice administered at dosing times) or any type of medication (other than acetaminophen, ibuprofen, birth-control pills, or Dexedrine) for the duration of the protocol. Subjects were asked to reduce significantly or eliminate completely caffeine consumption beginning several days prior to the study (although none of the subjects reported normally using substantial amounts of caffeine). Five of the six subjects were nonsmokers. The average total flight time was 748 hours.

Apparatus

Drug dosing

At each dose interval, subjects were administered orally two orange gelatin capsules with approximately eight ounces of orange juice. Each of the placebo capsules were filled with lactose, and each of the Dexedrine capsules contained 1 5-mg Dexedrine tablet placed in the lactose powder. There was no difference in the appearance of the placebo and Dexedrine capsules.

Vital signs data

Oral temperatures were collected with an IVAC thermometer (Model number 811)*. Pulse and blood pressure data were collected either with a Critikon vital signs monitor (Model number 1846SX)* or a conventional sphygmomanometer. An initial 12-lead EKG was taken with a Marquette microcomputer augmented cardiograph system.

*See list of manufacturers

UH-60 flight simulator

All simulator flights were conducted on site at the U.S. Army Aeromedical Research Laboratory (USAARL) at Fort Rucker, Alabama, using the UH-60 research flight simulator. This motion-base system is a full-visual simulator in which the computer-generated visual display was set for standard daytime flight. The simulator is equipped with a multichannel data acquisition system.

Flight data were acquired on a Digital Equipment Corporation VAX 11/780* interfaced to a Perkin-Elmer digital computer* which controlled the UH-60 flight simulator. This system monitored a variety of aspects of simulator control, including heading, airspeed, and altitude control, global positioning system (GPS) readouts, switch positions, and operator console inputs. The acquired data were converted to root mean square (RMS) errors using specialized software routines developed at USAARL (Jones and Higdon, 1991).

EEG evaluations

The electroencephalographic (EEG) evaluations conducted during each subjects' waking periods were performed with a Cadwell Spectrum 32, neurometric analyzer*. Twenty-one channels of EEG data were collected and stored on optical disk for subsequent analysis. The low filter was set at 0.53 Hz, the high filter was set at 70 Hz, and the 60 Hz notch filter was used. Subjects were outfitted with 25 Grass E5SH* silver cup electrodes which were affixed to the scalp with collodion for the duration of the study. All active EEG channels were referenced to linked mastoids (A1 and A2).

Desktop flight simulation task

A desktop flight simulation program (Microsoft Flight Simulator 4.0®)*, combined with a custom-designed, timed flight course (Microsoft Aircraft and Scenery Designer®)* was used as an additional surrogate for flight performance. This task was run on a 486 computer with VGA graphics. Flight control was via a realistic flight yoke (Virtual Pilot, CH Products®)*, with system interface using either mouse or keyboard, according to individual subject preference.

In addition to the primary "flight" task, subjects 2-6 were presented with a secondary task which was controlled from a Coulbourn modular instrument system*. This task presented a series of 6000 Hz and 5500 Hz tones separated by a 10-second interstimulus interval. It was the subject's task to press a yoke-mounted pushbutton as quickly as possible each time she heard the low-pitched tone (the maximum allowable response time was 5 seconds). The probability of the low tone was set at 40 percent. Response times were printed automatically.

Profile of mood states

Subjective evaluations of changes in mood were made with the Profile of Mood States (POMS) (McNair, Lorr, and Droppleman, 1981). The POMS is a 65-item paper and pencil test which measures affect or mood on 6 scales: 1) tension-anxiety, 2) depression-dejection, 3) anger-hostility, 4) vigor-activity, 5) fatigue-inertia, and 6) confusion-bewilderment. The answers were scored by using manual scoring templates.

Synthetic work battery

Assessments of basic cognitive abilities were made with the synthetic work environment (Elsmore, 1991). This task consisted of a Sternberg memory task, an arithmetic task, a visual monitoring task, and an auditory monitoring task. The synthetic work battery was administered via a computer interfaced with a mouse and a 13-inch color monitor.

Polysomnography

Evaluations of sleep quality as a function of drug were made during subjects' sleep periods using a Nihon Kohden electroencephalograph (model No. EEG-4321P)*. The EEG data were collected using a subset of the same electrodes attached for the recording of the waking EEG (C3, C4, O1, O2, A1, and A2). Four additional electrodes (SensorMedics)*, affixed with adhesive collars immediately prior to each sleep period, were used to collect electrooculographic (EOG) and electromyographic (EMG) data. The time constant for the EEG channels was set at 0.3 and the high filter was set at 35 Hz. For EOG (recorded from the outer canthus of each eye), the time constant was 5.0 and the high filter was set at 10 Hz. For EMG (recorded with submental

electrodes), a time constant of 0.003 and a high filter setting of 120 Hz were used. The 60 Hz notch filter was not employed.

Procedure

Each subject completed several simulator flights, electrophysiological evaluations, surrogate flight tasks, cognitive tests, and questionnaires under Dexedrine and placebo. The dose-administration schedule was fully counterbalanced, and neither the subjects nor the experimenters were informed about the order of drug/placebo administration. Testing was scheduled for most of the time the subject was awake.

Flight performance

The flight performance evaluations required subjects to perform the maneuvers listed in Table 1. There were three parts to each flight. The first part consisted of tactical navigation in which the subject was required to use visual cues, GPS information, and time information to correctly navigate a prescribed course. The second part consisted of nontactical, upper-airwork in which the subject was required to perform precision maneuvers based upon instrument information. The third part consisted of nap-of-the-earth (NOE) flight in which the subject was required to follow a leadship during flight at altitudes close to the earth over a prescribed course. The same sequence of maneuvers was used for every subject during each of the flights. These maneuvers were of the type typically flown in a UH-60 aircraft, and they are fully described in the Aircrew training manual (Department of the Army, 1988).

The low-level navigation portion of the profile began with four hovers. There was a straight 10-foot hover, a 10-foot hovering turn (360°), a stationary 40-foot hover, and a 40-foot hovering turn. These maneuvers were followed by the subject flying to five different check points using the global position system (GPS).

During the straight hovers, subjects were required to maintain precise control over both altitude and heading, whereas during the hovering turns subjects focused primarily on altitude control. During the low-level navigation, subjects were required to maintain proper control of altitude, slip, and roll while minimizing the deviation between their actual heading and the bearing to the next checkpoint.

Table 1.
Simulator flight maneuvers.

Maneuver	Description
1. Low hover	Maintain heading 150°, altitude 10 ft
2. Low hover turn	Heading from 150° to 330° while holding altitude of 10 ft above ground level
3. High hover	Maintain heading 330°, altitude 40 ft
4. High hover turn	Heading from 330° to 150°, while holding altitude of 40 ft above ground level
5. Navigate to chkpt 1	Maintain GPS heading within 10° Maintain 700 ft MSL within 100 ft Arrive at checkpoint in 3 min
6. Navigate to chkpt 2	Maintain GPS heading within 10° Maintain 600 ft MSL within 100 ft Arrive at checkpoint in 2 min
7. Navigate to chkpt 3	Maintain GPS heading within 10° Maintain 600 ft MSL within 100 ft Arrive at checkpoint in 5 min
8. Navigate to chkpt 4	Maintain GPS heading within 10° Maintain 600 ft MSL within 100 ft Arrive at checkpoint in 2 min
9. Navigate to chkpt 5	Maintain GPS heading within 10° Maintain 700 ft MSL within 100 ft Arrive at checkpoint in 4 min
10. Transition	Establish heading 360°, airspeed 120 k, altitude 2000 ft MSL
11. Straight & level	Maintain the above parameters 1 min
12. Left std rt Turn	Perform 360° left standard rate turn maintaining airspeed and altitude
13. Straight & level	Maintain heading 360°, airspeed 120 k, and altitude 2000 ft MSL for 1 min

Table 1 (continued)

Maneuver	Description
14. Climb	Climb from 2000 to 2500 ft while maintaining heading and airspeed (1 min)
15. Right std rt turn	Perform 180° right standard rate turn maintaining airspeed and altitude
16. Straight & level	Maintain heading 180°, airspeed 120 k, and altitude 2500 ft MSL for 1 min
17. Right std rt turn	Perform 180° right standard rate turn maintaining airspeed and altitude
18. Climb	from 2500 to 3500 ft while maintaining heading and airspeed
19. TURN AFCS OFF	----------
20. Descend	Descend from 3500 to 3000 ft while maintaining heading and airspeed
21. Left des std rt turn	Perform 180° left standard rate turn while descending from 3000 to 2500 ft maintaining airspeed
22. Descend	Descend from 2500 to 2000 ft while maintaining heading and airspeed
23. Left std rt turn	Perform 180° left standard rate turn maintaining altitude and airspeed
24. Straight & level	Maintain heading 360°, airspeed 120 k, altitude 2000 ft for 2 min
25. Right std tt turn	Perform 360° right standard rate turn while maintaining altitude and airspeed
26. Descend	Descend from 2000 to 1000 ft MSL maintaining heading and airspeed
27. TURN AFCS ON - MOVE TO COORDINATES	

Table 1 (continued)

Maneuver	Description
28. Execute terrain flt Approach to LZ	Maintain airspeed until approach angle intercept; touch down in Y zero ground speed
29. Perform formation flt takeoff (staggered left)	Maintain 3 rotor disk separation at 30° angle of lead ship. Depart ground simultaneously with lead ship
30. Perform formation flt (staggered left)	Maintain 3 rotor disk separation at 30° angle; maintain altitude and airspeed
31. Perform formation flt (trail)	Maintain 3 rotor disk separation behind lead ship; maintain altitude and airspeed
32. Perform formation flt approach (trail)	Maintain 3 rotor disk separation behind lead ship; touch down with lead

The upper-airwork part of the profile consisted of several standardized maneuvers which the subjects were required to fly in a specific order during each of their training and test flights. The first group of maneuvers was flown with the automatic flight control system (AFCS) trim engaged (the normal mode when flying the UH-60), and the second group was flown with the AFCS trim turned off. The AFCS trim system enhances the static stability and handling qualities of the aircraft/simulator.

There were 15 maneuvers in the upper-airwork profile. These consisted of four straight-and-levels (1 with AFCS off), two left standard-rate turns (1 with AFCS off), three right standard-rate turns (1 with AFCS off), two standard-rate climbs, three standard-rate descents (all with AFCS off), and one left descending turn (with AFCS off).

For each of these upper-airwork maneuvers, the subjects were required to maintain a constant airspeed of 120 knots, but the specific targets for other parameters such as heading, altitude, roll, slip, etc. varied depending upon which maneuver was being flown. However, subjects attempted to maintain appropriate ideal flight parameters during each maneuver. The specific maneuvers, the measures examined, and the ideal parameters for each are presented in Tables 2 and 3.

Table 2.
Upper airwork maneuvers (conducted with the AFCS on) with parameters scored for each maneuver.

Maneuver	Duration (sec)	Parameters	Ideal Values
Straight & Level	60	Heading	360 degrees
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Roll	0 degrees
Left Std Rate Turn	120	Turn rate	3 deg/sec
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	20 degrees
Straight & Level	60	Heading	360 degrees
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Roll	0 degrees
Climb	60	Heading	360 degrees
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	0 degrees
		Rate of Climb	500 feet/min
Right Std Rate Turn	60	Turn rate	3 deg/sec
		Altitude	2500 feet MSL
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	20 degrees
Straight & Level	60	Heading	180 degrees
		Altitude	2500 feet MSL
		Airspeed	120 knots
		Roll	0 degrees
Right Std Rate Turn	60	Turn rate	3 deg/sec
		Altitude	2500 feet MSL
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	20 degrees

Table 2 (continued)

Maneuver	Duration (sec)	Parameters	Ideal Values
Climb	60	Heading	360 degrees
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	0 degrees
		Rate of Climb	500 feet/min

Table 3.
Upper airwork maneuvers (conducted with the AFCS off) with parameters scored for each maneuver.

Maneuver	Duration (sec)	Parameters	Ideal Values
Descent	60	Heading	360 degrees
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	0 degrees
		Rate of Descnt	500 feet/min
Left Descending Turn	60	Turn Rate	3 deg/sec
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	20 degrees
		Rate of Descnt	500 feet/min
Descent	60	Heading	180 degrees
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	0 degrees
		Rate of Descnt	500 feet/min
Left Std Rate Turn	60	Turn rate	3 deg/sec
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	20 degrees

Table 3 (continued)

Maneuver	Duration (sec)	Parameters	Ideal Values
Straight & Level	120	Heading	360 degrees
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Roll	0 degrees
Right Std Rate Turn	120	Turn rate	3 deg/sec
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	20 degrees
Descent	120	Heading	360 degrees
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	0 degrees
		Rate of Descnt	500 feet/min

The last part of the flight profile consisted of the subject following a lead ship through a standardized low-level course. There were four segments in this part of the profile, but only the middle two were graded. Specifically, subjects were evaluated on how well they followed the lead ship first in a 30-degree staggered-left configuration and then directly behind (trail formation). During both of these segments, the subjects were required to match the altitude of the lead ship while maintaining 3 rotor-disks of separation and a constant trail angle (30 degrees or directly behind the lead ship).

Root mean square (RMS) errors were calculated for each measure within each of the maneuvers (hovers, navigation, upper-airwork, and formation flight) in order to express how well subjects maintained specific headings, altitudes, air speeds, and other parameters. The formula for calculating RMS error is essentially the same as the formula for calculating a standard deviation with the exception that RMS errors reflect the amount of deviation from an ideal value rather than deviations from a mean. The RMS errors were transformed to their log natural values prior to analysis to minimize the influence of extreme scores.

The entire profile lasted approximately 1 hour, and during each profile, performance was measured using the simulator's computerized performance monitoring system which was described earlier. During each flight, a UH-60 pilot (acting as the console operator) was present to instruct the subject and ensure the proper sequencing and timing of all flight maneuvers.

EEG evaluations

Each EEG session lasted approximately 40 minutes and began with a check to ensure electrode impedances were 5000 Ohms or less. Any impedance problems were corrected by rotating a blunted needle gently inside of the problem electrode until an adequate signal was obtained. The subjects then were instructed to sit quietly with eyes closed for 1.5 m followed by 1.5 m of eyes opened while data were recorded. After the resting EEG, subjects were given a series of evoked potential tasks not reported here.

The EEGs for eyes-open and eyes-closed later were scanned visually for three relatively artifact-free 2.5-second epochs on which absolute power values were calculated for each of four bands. The results then were averaged together to produce one set of power values for each electrode site under eyes closed and eyes open. The activity bands were defined as follows: delta (1.5-3.0 Hz), theta (3.0-8.0 Hz), alpha (8.0-13.0 Hz), and beta (13.0-20.0 Hz).

Desktop flight simulation task

Following the EEG, subjects completed a 30-minute session on the desktop flight simulation task. This task required subjects to fly a timed course consisting of 21 "gates" positioned at various altitudes and headings. The first 15 gates were flown under nonturbulent conditions while gates 16-21 were made more difficult by the addition of 20-knot winds emanating from various directions. In addition, a secondary task involved the presentation of high- and low-pitched tones at 20-second intervals throughout the task, and the subject was required to press a button immediately following the presentation of each low-pitched tone.

The primary surrogate flight task produced a summary score at the conclusion of each "flight." The score was calculated automatically from the elapsed time it took to fly the course,

the number of gates missed, and the precision with which the subjects flew through each of the gates. The secondary task produced mean reaction times to the low-pitched target tones and the number of errors (false presses and omitted presses). These results were stratified into wind/nonwind levels of difficulty for analysis.

Profile of Mood States

The POMS was given immediately after each flight simulation test. Subjects were presented with a series of 65 words which described mood states, and for each "mood state" the subject indicated on a standardized answer sheet how well it described the way she presently was feeling. This test took approximately 5 minutes to administer, and yielded scores on the factors of tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment.

Cognitive performance evaluations

Following the POMS, subjects completed a 10-minute session on the synthetic work environment. This test required subjects to simultaneously monitor and respond to four tasks which were presented on four quadrants of the computer screen. In the upper left quadrant, there was a Sternberg memory task which briefly presented the subject with a 6-letter memory set and subsequently required her to indicate whether or not a series of individually presented single letters (probes) had been present in the initial list. In the upper right quadrant, there was a 3-column arithmetic task which required the subject to perform additions on 2 numbers (each less than 1000). In the lower left quadrant, there was a visual monitoring task in which the subject monitored a pointer moving from center to either end of a scale. The subject was required to reset the pointer to its center position prior to its reaching the end. In the lower right quadrant, there was an auditory monitoring task which required the subject to indicate when a high tone had been presented among several low tones. All responses were made via a mouse to avoid any distraction from attempting to locate response keys on the keyboard. This test yielded a variety of speed and accuracy scores for each task.

Polysomnography

The sleep recordings were made while the aviator was sleeping in a darkened, private bedroom. Each night on which sleep was allowed (adaptation, baseline, recovery-1, and recovery-2), the EOG and submental electrodes were placed, the subject was escorted into her bedroom at the proper time, the electrodes were plugged into the preamplifier, and the signal quality was checked. After the system was verified, the lights were turned out at approximately 2300, and the subject was permitted to sleep while electrophysiological data were recorded. A chart speed of 10 mm per second was used.

There were 3 nights during which polysomnographic data were collected. The first was a baseline night that occurred on Monday (following a Sunday adaptation night). The second was the recovery night on Wednesday, and the third was the recovery night on Friday. Data from each of these nights were recorded on a standard paper trace and scored according to the rules set forth by Rechtschaffen and Kales (1968).

The number of minutes from lights out to the appearance of stage 2 sleep, the latency until the first REM period, the percentage of time subjects spent in stages 1-4 and REM sleep, the percentage of movement time, and the percentage of time subjects were awake during the night were calculated.

Test schedule

The test schedule is depicted in Table 4. Check-in time at the Laboratory was approximately 1800 on Sunday, at which point the study was explained, the informed consent agreement was signed, and the medical evaluation was conducted. The medical evaluation consisted of a medical records review, completion of a medical questionnaire, and a physical examination which included a 12-lead EKG. Subjects with evidence of past psychiatric or cardiac disorder, allergic reactions to aspirin, a history of sleep disturbances, or any current significant illness would have been rejected, but none of these problems were identified in any of the volunteers. One of the subjects was found to have a long-standing hepatitis B condition, but this was not considered relevant to the present study.

Table 4.
Testing schedule.

TIME	SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
00-01				**DEX/PBO**		**DEX/PBO**	
01-02				simulator		simulator	
02-03		s l e e p	s l e e p	eeg	s l e e p	eeg	s l e e p
03-04				minisim poms		minisim poms	
04-05				**DEX/PBO**		**DEX/PBO**	
05-06				simulator		simulator	
06-07				eeg		eeg	
07-08		wake up	wake up	minisim poms	wake up	minisim poms	wake up breakfast RELEASE
08-09		**testdose** breakfast	breakfast	**DEX/PBO** breakfast	breakfast	**DEX/PBO** breakfast	
09-10		simulator	simulator	simulator	simulator	simulator	
10-11		eeg	eeg	eeg	eeg	eeg	
11-12		minisim	minisim poms	minisim poms	minisim poms	minisim poms	
12-13		poms lunch	lunch	lunch	lunch	lunch	
13-14		simulator	simulator	simulator	simulator	simulator	
14-15		eeg	eeg	eeg	eeg	eeg	
15-16		minisim	minisim poms	minisim poms	minisim poms	minisim poms	
16-17		poms					
17-18		simulator	simulator	simulator	simulator	simulator	
18-19	ARRIVE med exam	eeg	eeg	eeg	eeg	eeg	
19-20		minisim poms	minisim poms	minisim poms	minisim poms	minisim poms	
20-21	eeg hookup						
21-22		dinner pt	dinner pt	dinner pt	dinner pt	dinner pt	
22-23	freetime	shower poms	shower	shower poms	shower	shower poms	
23-24	bed time	bed time	poms	bed time	poms	bed time	

Note: DEX = Dexedrine dose (10 mg), PBO = Placebo

After completion of the physical examination, the subjects's head was measured and electrodes were attached according to the International 10-20 guide. The subject then was free to relax until bedtime (2300 hours).

On Monday morning, the subject was given a 2.5 mg dextroamphetamine test dose. Afterward, there were three simulator training flights followed by three EEG, performance, and mood testing sessions. At 2100 hours, the aviator participated in physical exercise, and at 2300 hours she retired for the day. On Tuesday, there were three baseline simulator flights and three EEG, performance, and mood baseline tests. Every activity which occurred on Monday was repeated on Tuesday with the exception that the aviator was not allowed to go to sleep at 2300. Instead, she was given her first drug/placebo dose at 2400 hours, and subsequent doses were given at 0400 and 0800 on Wednesday. Simulator testing began 1 hour after each drug/placebo administration (for the first three sessions) followed by two additional nondrug sessions as well. Other tests followed each simulator flight--just as on previous days. Thus, there was a total of 5 equally-spaced test sessions completed on this day (at 0100, 0500, 0900, 1300, and 1700). Afterwards, the subject ate dinner, exercised, and retired for the day. On Thursday, the subject repeated the same schedule which was used on Tuesday. There were three test sessions during the day, and, as was the case on Tuesday night, the subject was not allowed to go to bed at 2300. Instead she was given the first dose in her second series of drug/placebo doses at 2400. On Friday, the subject repeated the Wednesday schedule, beginning her simulator flight at 0100 and completing the other sessions at 4-hour intervals until 2000. At 2300 hours, she retired for the day. On Saturday, the subject was awakened at 0700 and prepared for departure from the Laboratory. She was examined by the flight surgeon (and given a written medical recommendation for return to flying duty) before being released to travel home.

Results

General

The objective of this research was to assess the efficacy of using Dexedrine to sustain female UH-60 helicopter pilot performance during periods of sleep deprivation. The data from the two deprivation periods were analyzed to compare both the magnitude and time-course of Dexedrine's effects relative to

placebo. Thus, the analyses each consisted of at least the 2 primary factors of drug (Dexedrine versus placebo) and session (0100, 0500, 0900, 1300, and 1700).

Flight performance data

BMDP 4V (Dixon et al., 1990) was used to conduct a series of repeated measures analyses of variance (ANOVAs) on the transformed RMS errors from each maneuver in the flight profile. The first 2 within-subjects factors for each maneuver were drug (Placebo, Dexedrine) and session (0100, 0500, 0900, 1300, and 1700). Maneuvers which were flown more than once during each flight profile included a third factor designated iteration. There were two iterations of straight hovers, two iterations of hovering turns, four navigation legs, four straight-and-levels, three right-standard-rate turns and descents, and two left-standard-rate turns and climbs. Significant main effects and interactions from these ANOVAs were followed by appropriate posthoc analyses consisting of simple effects and/or contrasts to pinpoint the location of noteworthy differences.

There was missing flight performance data from the 1300 session on the sixth subject's Dexedrine administration day due to a power failure in the Laboratory. This subject also was missing the last descent at 0100 on the Dexedrine administration day, and subject number 2 was missing the first left standard-rate turn from the 1700 session on the same day (reasons for both of these were unclear). These data were estimated using BMDP AM in which the means of existing data were substituted for missing data.

The trail formation portion of each subject's flights were not analyzed in the present investigation because, as a group, subjects were unable to establish asymptotic performance on this part of the flight. Apparently, very few of the pilots routinely performed formation flights in their operational assignments, and this made rapid training impossible.

Hovers

The 3-way ANOVA (drug x session x iteration) on how well the subjects controlled heading and altitude during the 10-foot and 40-foot stationary hovers indicated there were no interactions or main effects for this maneuver. The ANOVA on how well subjects controlled altitude during the 10-foot and 40-foot hovering turns

similarly indicated no significant interactions. However, there was a main effect on the iteration factor ($F(1,5)=130.27, p=.0001$) which was because altitude control was more variable during the 40-foot hover than during the 10-foot hover.

Low-level navigation

The ANOVA on how well the subjects maintained correct headings, altitudes, slip, and roll control while using the GPS to navigate the low-level course revealed several effects. First, there was a drug-by-session interaction on heading control ($F(4,20)=6.08, p=.0023$). Second, there were iteration main effects on heading ($F(3,15)=7.91, p=.0021$), altitude ($F(3,15)=3.64, p=.0375$), slip ($F(3,15)=12.17, p=.0003$), and roll control ($F(3,15)=38.35, p<.0001$). Third, there were drug main effects on both heading ($F(1,5)=30.12, p=.0027$) and altitude control ($F(1,5)=20.69, p=.0061$).

The drug-by-session interaction was due to differences between heading RMS errors under Dexedrine in comparison to placebo at 0900, 1300, and 1700 ($p<.05$), but not at 0100 and 0500. In every case where there was a difference between the two drug conditions, performance was better under Dexedrine than under placebo (see figure 1).

The iteration main effect on heading, slip, and roll control (see figure 2) was due to better performance on the fourth navigation leg than on the third, with better performance on the second leg than the third as well ($p<.05$). In addition, heading, slip, and roll control were all better on the first navigation leg than on the third. However, heading and roll control on the first leg were worse than heading control on the fourth ($p<.05$). Altitude control was better on the first than the second leg, whereas roll control was worse on the first leg than the second ($p<.05$).

The drug main effect on heading control resulted from significantly better performance under Dexedrine than under placebo. The same Dexedrine-related enhancement occurred on altitude control. The mean RMS errors for heading were 1.3 degrees under Dexedrine versus 1.8 degrees under placebo, and the mean altitude errors were 14.7 feet versus 18.8 feet, respectively.

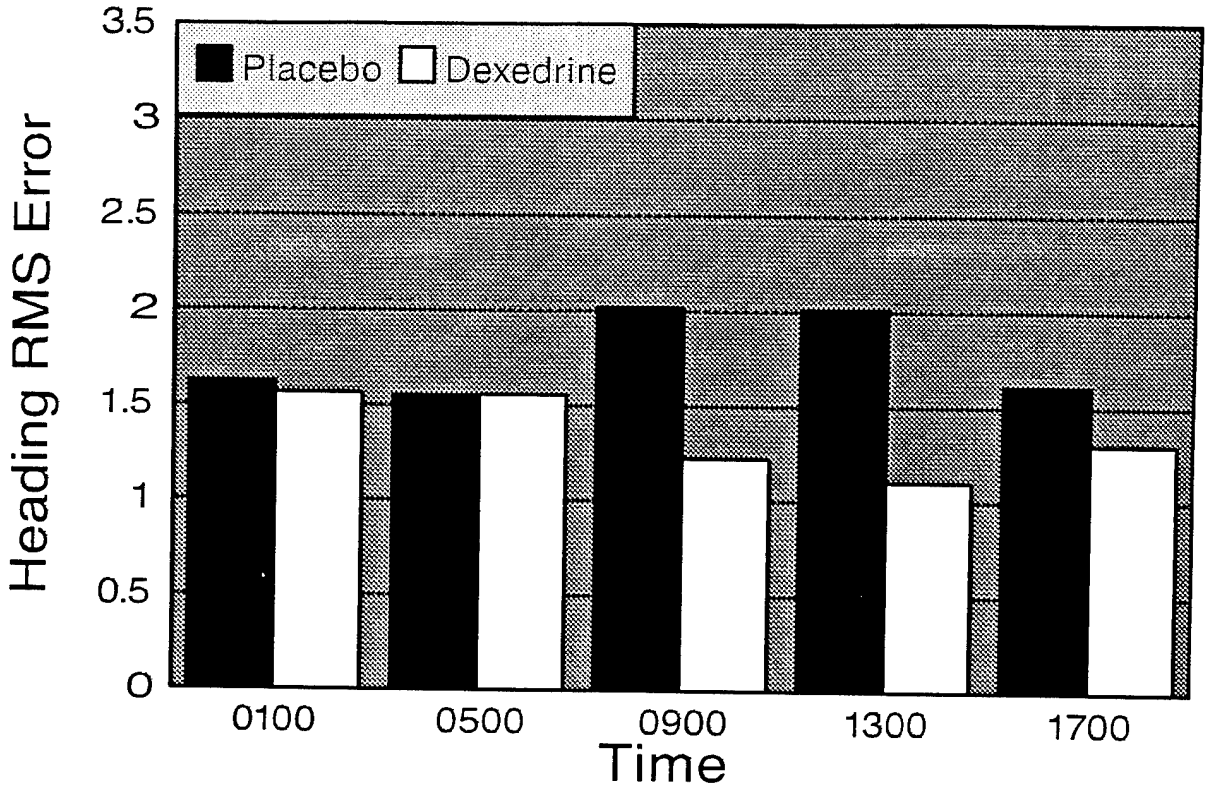


Figure 1. Effects of drug and session on heading control during low-level navigation.

Straight and levels

The 3-way analysis of variance (drug x session x iteration) conducted on heading, airspeed, altitude, slip, and roll control during the four straight-and-level (SL) maneuvers indicated there were several interactions and main effects. There was a significant 3-way interaction on altitude control ($F(12,60)=6.34, p<.0001$) which analysis of simple effects indicated was due to drug-by-session interactions at SL 3 and SL 4 ($p<.05$), but not at SLs 1 and 2. The interaction at SL 3 was because of poorer performance under Dexedrine than placebo at 0100 and 1700 while there was better performance under Dexedrine than placebo at 0900 ($p<.05$). The interaction at SL 4 (with no AFCS trim) was due to better performance under Dexedrine than placebo at 0900 ($p<.05$), whereas there were no differences between the 2 drug conditions at any of the other sessions. These effects are depicted in figure 3.

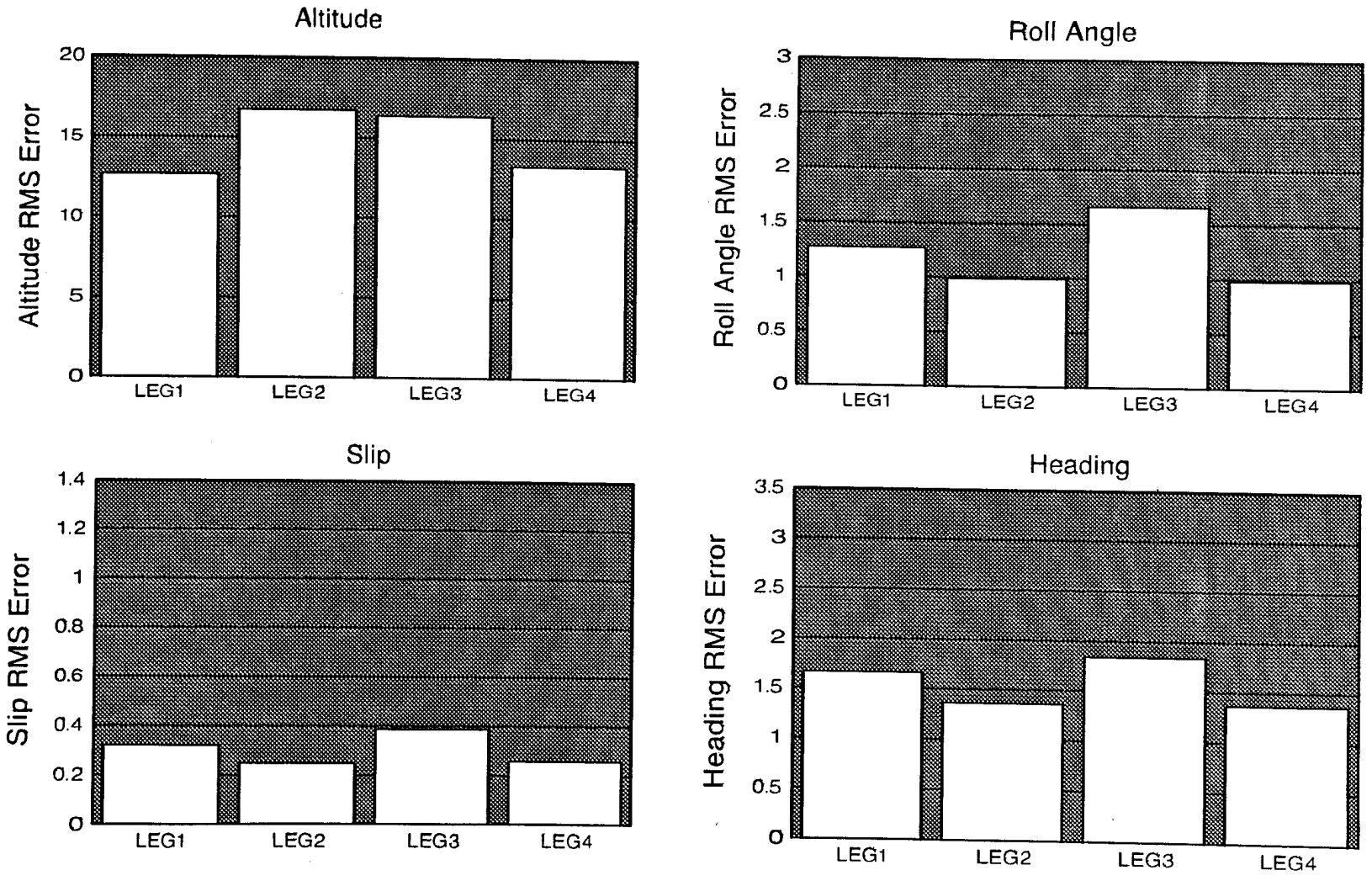


Figure 2. Differences among various low-level navigation segments (legs) on altitude, roll angle, slip, and heading.

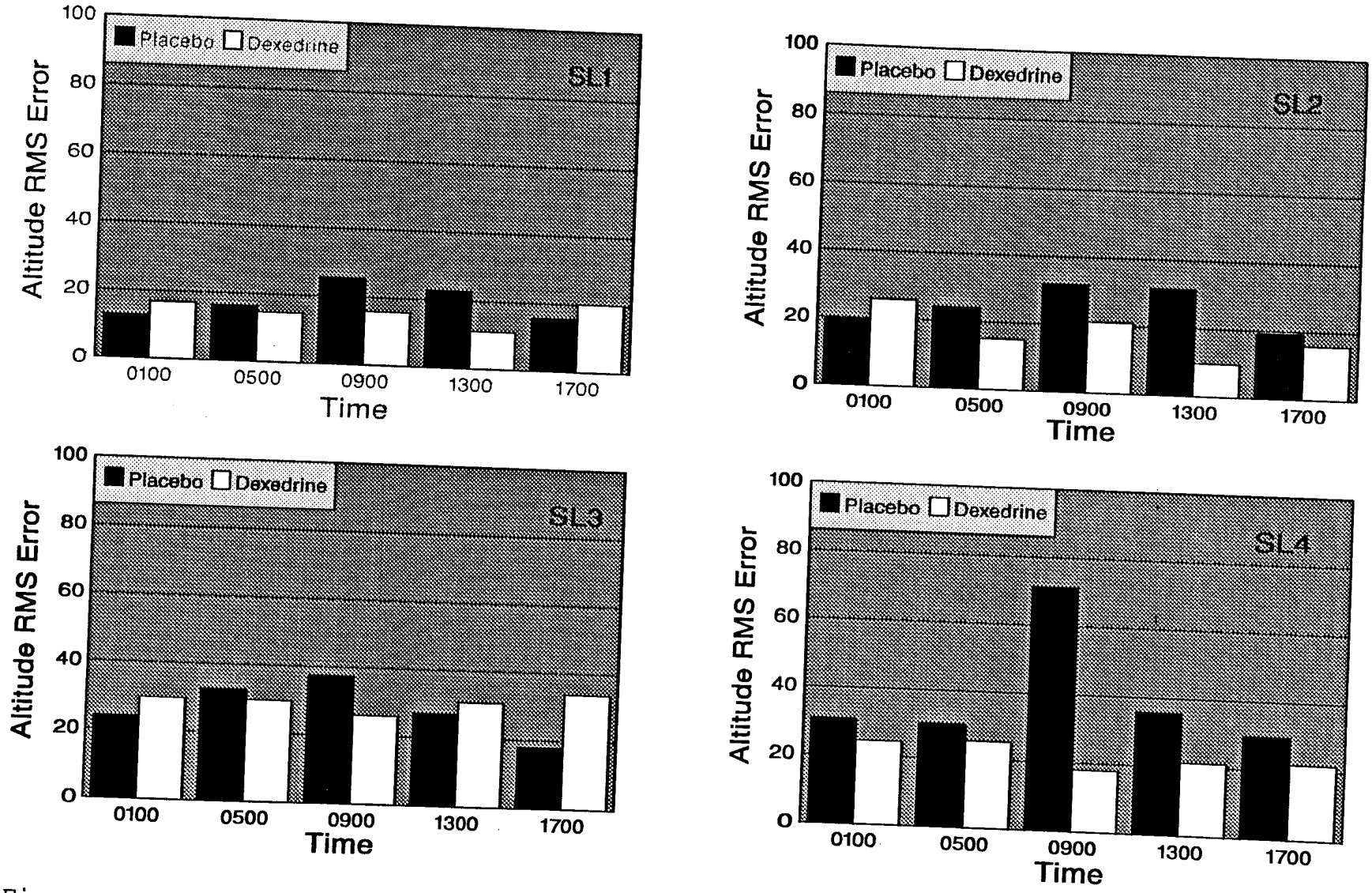


Figure 3. Effects of drug and session on altitude control during each of the four straight-and-levels.

There was a session-by-SL interaction on altitude control ($F(12,60)=6.47, p<.0001$). Followup analyses of simple effects showed overall differences among the flights (sessions) at SLs 2 and 3 ($p<.05$) with no similar effects at SLs 1 and 4. The session effect at SL 2 was due to better altitude control at 1700 than at 0100 or 0900. Also, performance was better at 1300 than it was at 0900 ($p<.05$). The session effect at SL 3 was due to better altitude control at 0100 than at 0500, 0900, or 1300 ($p<.05$).

There was a drug-by-SL interaction on airspeed control ($F(3,15)=4.21, p=.0239$) which was due to a difference between Dexedrine and placebo at SL 4 ($p<.05$) that was not present at SLs 1-3 (see figure 4). An examination of the mean airspeed RMS errors at this last iteration of SL (with no trim) showed that Dexedrine was associated with better performance than placebo.

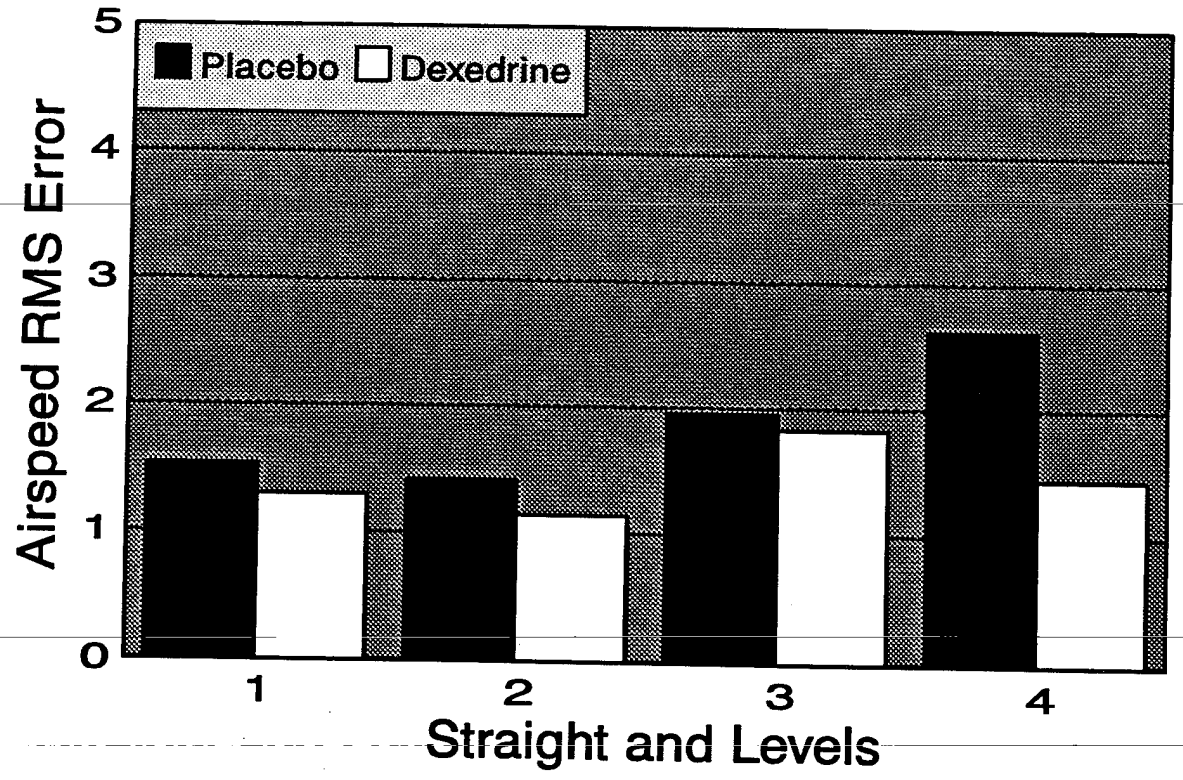


Figure 4. Effects of drug and straight-and-level on airspeed control.

In addition to these interactions, there were significant main effects on iteration, session, and drug. The iteration main effects were found on heading ($F(3,15)=10.08, p=.0007$), altitude ($F(3,15)=5.46, p=.0097$), airspeed ($F(3,15)=8.90, p=.0013$), and roll control ($F(3,15)=29.10, p<.0001$). With the exception of airspeed control, performance was better during SL 1 than during SLs 2-4 on every measure ($p<.05$). In addition, performance was better during SL 2 than during SL 4 on each of these parameters. On heading and roll control, performance was better during SL 3 than during SL 4 ($p<.05$) as well. With regard to airspeed control, performance was better on SLs 1 and 2 than it was on SLs 3 or 4 ($p<.05$).

The session main effects were found on altitude control ($F(4,20)=11.15, p=.0001$), and marginally on airspeed control ($F(4,20)=2.77, p=.0555$). Posthoc contrasts indicated the session effect on altitude was a result of better performance at 1700 than at any of the previous sessions ($p<.05$). The marginal session effect on airspeed was due to better performance at 1700 than at 0900 ($p<.05$) while there were no differences elsewhere.

The drug main effects were found on altitude control ($F(1,5)=13.24, p=.0149$), and marginally on airspeed control ($F(1,5)=6.06, p=.0571$). In both cases, performance was better under Dexedrine than it was under placebo. The mean RMS errors for altitude were 21.3 feet under Dexedrine versus 27.8 feet under placebo, and the mean errors for airspeed were 1.4 knots versus 1.9 knots, respectively.

Left standard-rate turns

The two left standard-rate turns (with and without AFCS) were analyzed in a 3-way analysis of variance for drug, session, and iteration effects. The specific parameters evaluated were turn rate, altitude, airspeed, slip, and roll control.

The ANOVA indicated no 3-way interactions, but there were 2-way interactions. The first 2-way interaction was between drug and iteration on roll control ($F(1,5)=11.94, p=.0181$). Analysis of simple effects showed there were differences between the first and second turns both under placebo and Dexedrine ($p<.05$). However, the RMS errors from the first turn (with AFCS) to the second turn (without AFCS) under placebo evidenced a more pronounced increase than did the RMS errors between the first and

second turns under Dexedrine. The mean RMS errors under placebo were 0.82 for the first turn and 2.1 for the second turn, whereas the mean RMS errors under Dexedrine were 0.97 and 2.1 respectively.

The second 2-way interaction involved the drug and session factors on altitude control ($F(4,20)=3.96, p=.0159$). Analysis of simple effects revealed that altitude control was significantly better under Dexedrine than under placebo at 0500 and 0900 ($p<.05$), whereas there were no drug effects at any of the other sessions (see figure 5).

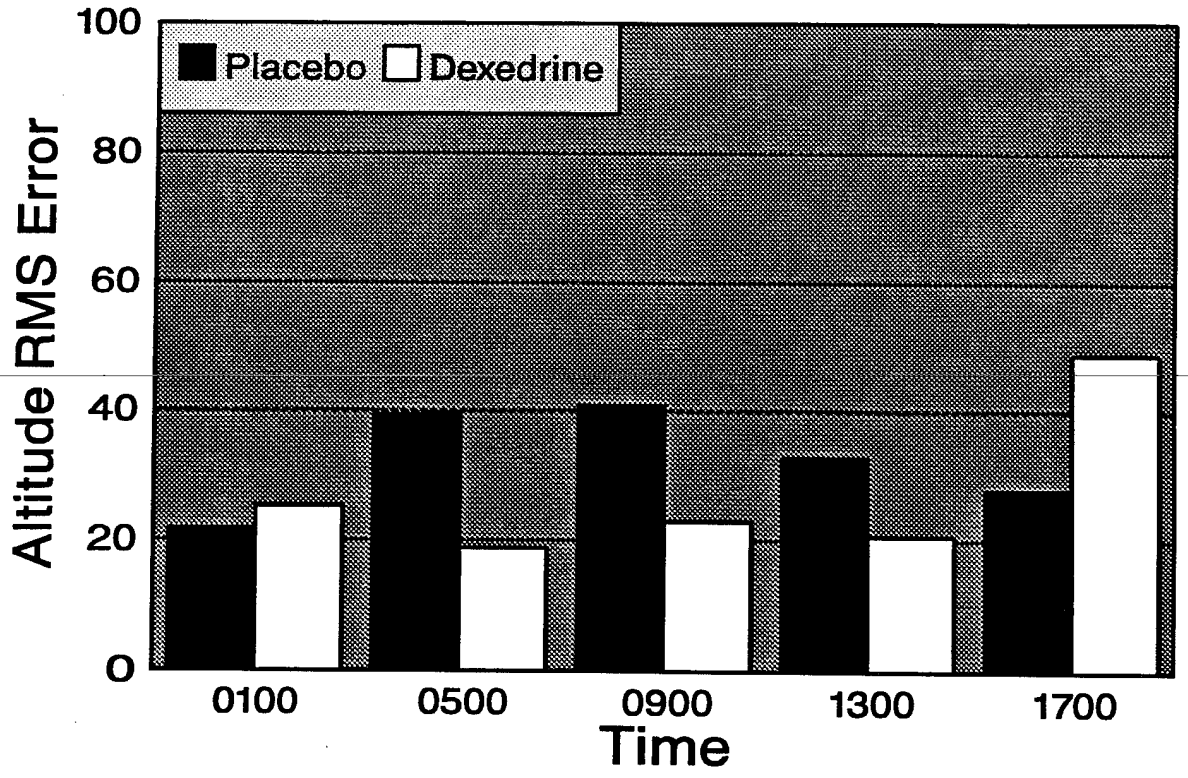


Figure 5. Effects of drug and session on altitude control during the left standard-rate turns.

There were overall differences between the first and second left-standard-rate turns on turn rate ($F(1,5)=91.07, p=.0002$), altitude control ($F(1,5)=14.08, p=.0133$), airspeed control ($F(1,5)=19.11, p=.0072$), slip control ($F(1,5)=33.71, p=.0021$), and roll control ($F(1,5)=42.05, p=.0013$). All of the differences resulted from subjects being able to fly more precisely during the first turn (with the AFCS engaged) than during the second turn (without AFCS).

There were differences among the 5 testing sessions only on turn rate ($F(4,20)=3.35, p=.0296$). Subsequent contrasts indicated this was due to poorer overall performance at 0900 than at either 0100 or 1700 ($p<.05$).

There were no significant main effects on the drug factor. However, there were tendencies ($p<.08$) for there to have been better altitude and airspeed control under Dexedrine (RMS errors of 21.3 feet and 1.4 knots) than placebo (27.8 feet and 1.9 knots). The tendency with regard to altitude control supports the drug-by-session interaction discussed earlier.

Climb

The two straight climbs were also evaluated with a 3-way ANOVA (drug x session x iteration) in terms of how well subjects maintained control over heading, airspeed, slip, roll, and rate of climb. Both climbs were conducted with the AFCS engaged.

There was no 3-way interaction, but 2-way interactions were found between drug and session on airspeed ($F(4,20)=3.81, p=.0185$) and rate of climb ($F(4,20)=5.05, p=.0056$). Both of these interactions were attributable to significant differences between performance under Dexedrine versus placebo at 0900 ($p<.05$), while there were no drug effects at the remaining sessions. At 0900, Dexedrine produced superior performance in comparison to placebo (see figure 6).

There were main effects on the iteration factor (first climb versus second climb) for heading ($F(1,5)=14.52, p=.0125$), airspeed ($F(1,5)=21.81, p=.0055$), slip ($F(1,5)=25.58, p=.0039$), roll ($F(1,5)=22.58, p=.0051$), and rate of climb ($F(1,5)=9.90, p=.0255$). In every case, there was poorer performance on the second climb (which lasted 120 seconds) than there was on the first climb (which lasted only 60 seconds).

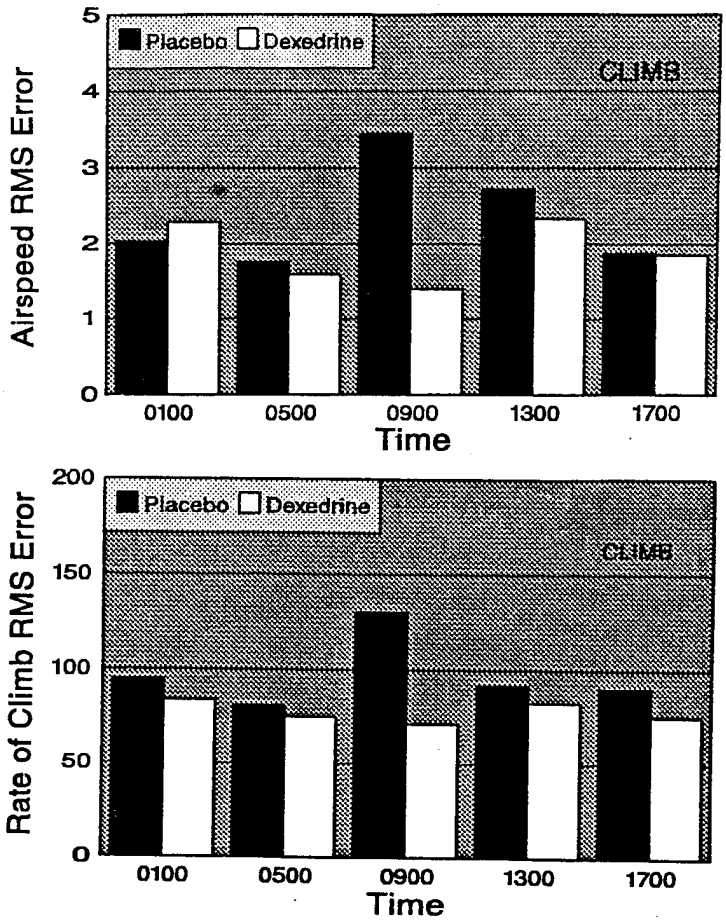


Figure 6. Effects of drug and session on airspeed control and rate-of-climb control during the climbs.

There also was a significant main effect on heading ($F(1,5)=9.64, p=.0267$) attributable to drug. This was because of better overall performance under Dexedrine than under placebo. The mean RMS error for heading under Dexedrine was 0.92 degrees versus 1.4 degrees under placebo.

Right standard-rate turns

The three right standard-rate turns (RSRTs) were evaluated in terms of how well subjects maintained an accurate turn rate, and how well they controlled altitude, air speed, slip, and roll during each drug condition, session, and iteration. The first and second RSRTs were flown with the AFCS trim engaged, and the third RSRT was flown with the AFCS trim off.

The ANOVA revealed no 3-way interactions, but there was a 2-way interaction between drug and session on airspeed control ($F(4,20)=3.23, p=.0338$). Analysis of simple effects indicated this was due to superior airspeed control under Dexedrine in comparison to placebo at 0900 and 1300 ($p<.05$); however, there were no differences at the other sessions (see figure 7).

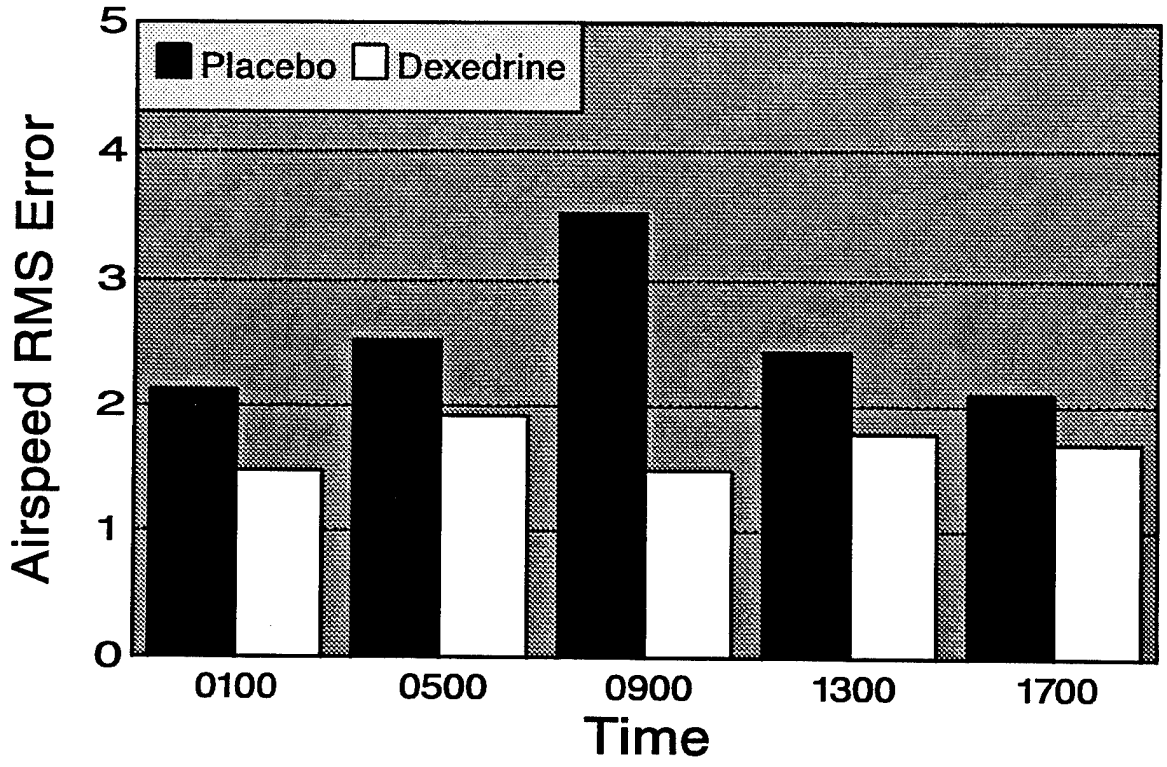


Figure 7. Effects of drug and session on airspeed control during the right standard-rate turns.

There were iteration main effects on turn rate ($F(2,10)=15.42, p=.0009$), airspeed ($F(2,10)=4.96, p=.0319$), slip ($F(2,10)=14.58, p=.0011$), and roll-angle control ($F(2,10)=30.44, p=.0001$). On all four parameters, performance was poorer on the third RSRT than it was on the second RSRT, and on turn rate and roll angle, the third RSRT was worse than the first

RSRT as well ($p<.05$). Slip control was affected differently in that performance on the first and third RSRTs was equivalent, while performance on the second RSRT was the best ($p<.05$).

There were drug main effects on both altitude ($F(1,5)=27.82, p=.0033$) and airspeed control ($F(1,5)=41.09, p=.0014$) which were due to better performance under Dexedrine than under placebo. The mean RMS errors for altitude (Dexedrine versus placebo) were 22.6 feet and 37.0 feet, and the errors for airspeed were 1.7 knots and 2.5 knots.

Descent

The three standard-rate descents were each examined in terms of how well subjects maintained designated heading, airspeed, slip, roll, and rate-of-descent parameters. All three iterations were flown with the AFCS trim turned off. The RMS errors for each measure were analyzed with a 3-way ANOVA (drug x session x iteration).

There were no 3-way interactions, but there were several 2-way interactions and several main effects. There were session-by-iteration interactions on roll ($F(8,40)=3.27, p=.0059$) and rate of descent ($F(8,40)=3.65, p=.0028$), both of which are depicted in figure 8. The interaction involving roll control was due to a difference among the sessions at the first descent ($p<.05$) while a similar effect did not occur within the second or third descents. Contrasts among the sessions within the first descent indicated that roll control was better at 0100 than at any of the remaining sessions and that roll control was better at 1300 than it was at 0900 ($p<.05$). The interaction involving rate-of-descent control was due to differences among the sessions at the first and third descents ($p<.05$) which were not present during the second descent. Subsequent contrasts on the rate-of-climb control during the first descent indicated that control was better at 0100 than it was at 0900, and control at 0500 was better than it was at 0900 or 1700 ($p<.05$). Contrasts on the rate-of-climb control during the third descent indicated that control was better at 0100 and 0500 than it was for any of the remaining sessions ($p<.05$); however, there was no difference between performance at 0100 and 0900.

There were drug-by-session interactions involving the control of heading ($F(4,20)=6.74, p=.0013$), roll ($F(4,20)=6.87, p=.0012$), and rate of descent ($F(4,20)=4.67, p=.0080$). Analysis of simple effects indicated

that in every case, significantly better performance was evident under Dexedrine than under placebo at 0900 ($p<.05$). In addition, there was better heading control under Dexedrine than under placebo at 0100 and 0500 as well ($p<.05$). These effects are shown in figure 9.

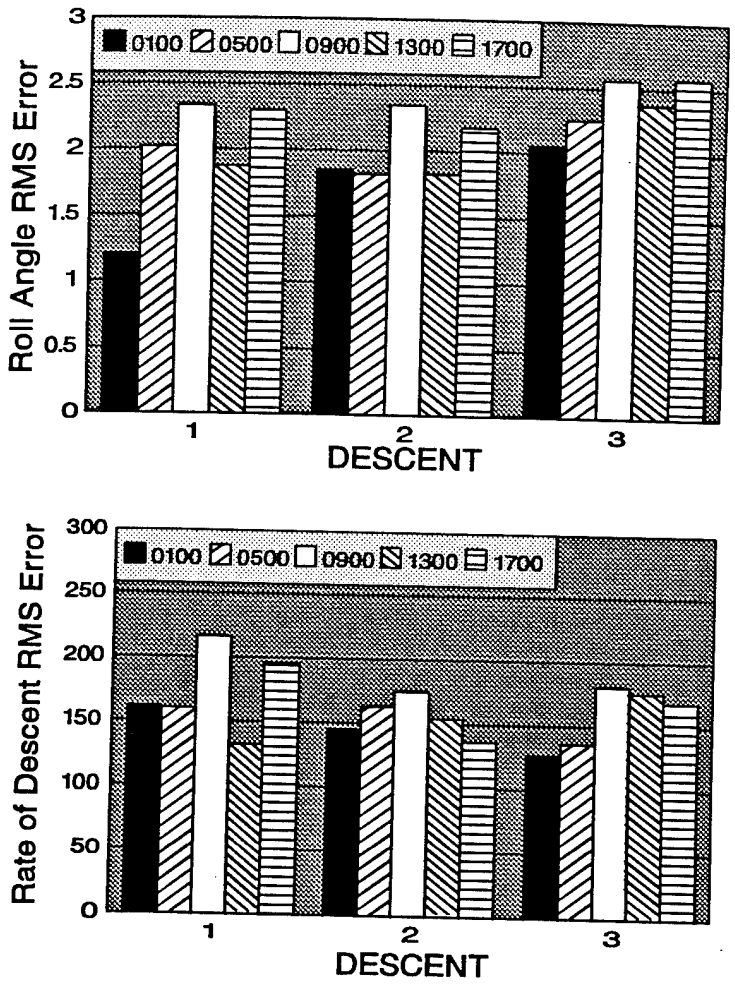
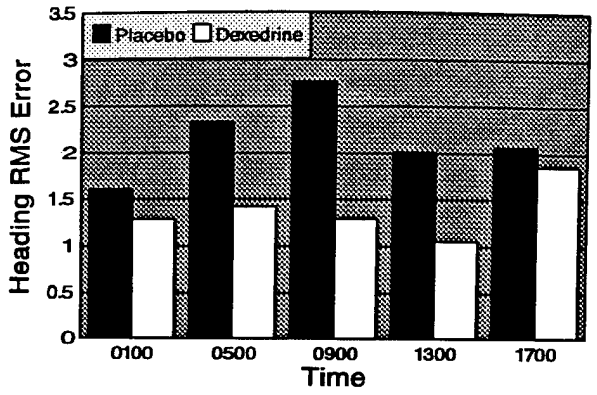
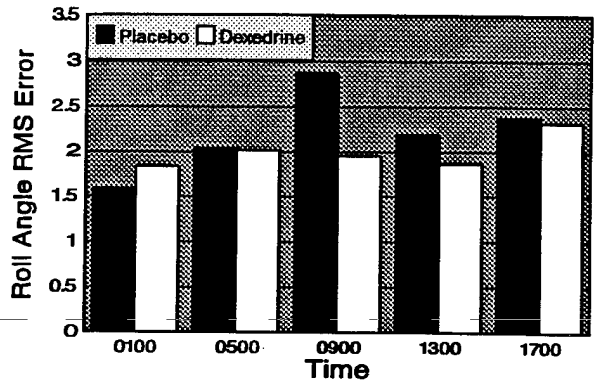


Figure 8. Effects of session and descent on roll angle and rate of descent.

There was one iteration main effect which indicated a difference among the three descents on roll control ($F(2,10)=4.57, p=.0389$). Contrasts showed a difference between the first and the third descents (the first was better than the third), but none of the other comparisons were significant.





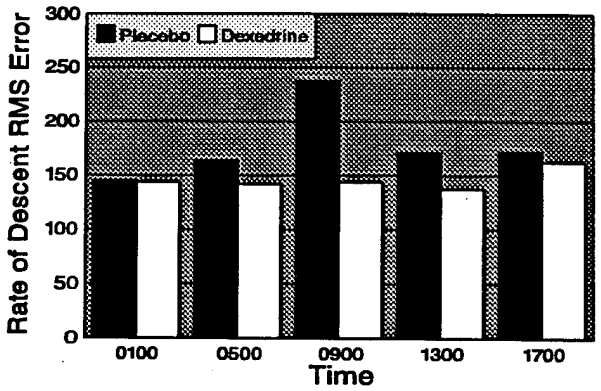


Figure 9. Effects of drug and session on heading, roll, and rate-of-descent control during the descents.

There were main effects on the session factor for heading ($F(4,20)=3.07, p=.0399$), slip ($F(4,20)=4.94, p=.0062$), and roll control ($F(4,20)=5.34, p=.0043$)--all of which are depicted in figure 10. Contrasts on heading indicated that control was better at 0100 than at 0900, but control was worse both at 0500 and 0900 than it was at 1300 ($p<.05$). In addition, heading control deteriorated at 1700 so that it was significantly worse than it was at either 0500 or 1300 ($p<.05$). Contrasts on slip indicated that slip control was better at 0100 than at 0500 or 0900, but slip control was worse at 0900 than it was at 1300 ($p<.05$). The contrasts on roll control were more straightforward in that they indicated roll control was better at 0100 than at any of the other sessions ($p<.05$).

There were also main effects on the drug factor which involved both heading ($F(1,5)=40.39, p=.0014$) and slip ($F(1,5)=6.28, p=.0540$). Both of these effects were due to better overall performance under Dexedrine than under placebo. The mean RMS error for heading under Dexedrine was 1.4 degrees versus 2.2 degrees under placebo, and the error for slip was 0.42 ball widths versus 0.54 ball widths under the respective drug conditions.

Left descending turn

There was only a single left-descending turn performed during the flight profile, and this maneuver was scored in terms of how well subjects were able to maintain a correct rate of turn, airspeed, slip, roll, and descent rate. The left descending turn was the second maneuver to be conducted once the AFCS was turned off. Results were analyzed in a 2-way ANOVA for drug and session.

The analysis indicated there was no drug-by-session interaction or session main effect. However, drug main effects were found for slip ($F(1,5)=22.82, p=.0050$) and rate of climb ($F(1,5)=7.01, p=.0456$). In both cases, performance was significantly better under Dexedrine (RMS errors of 0.9 ball widths and 160 feet per minute) than placebo (1.2 ball widths and 245 feet per minute).

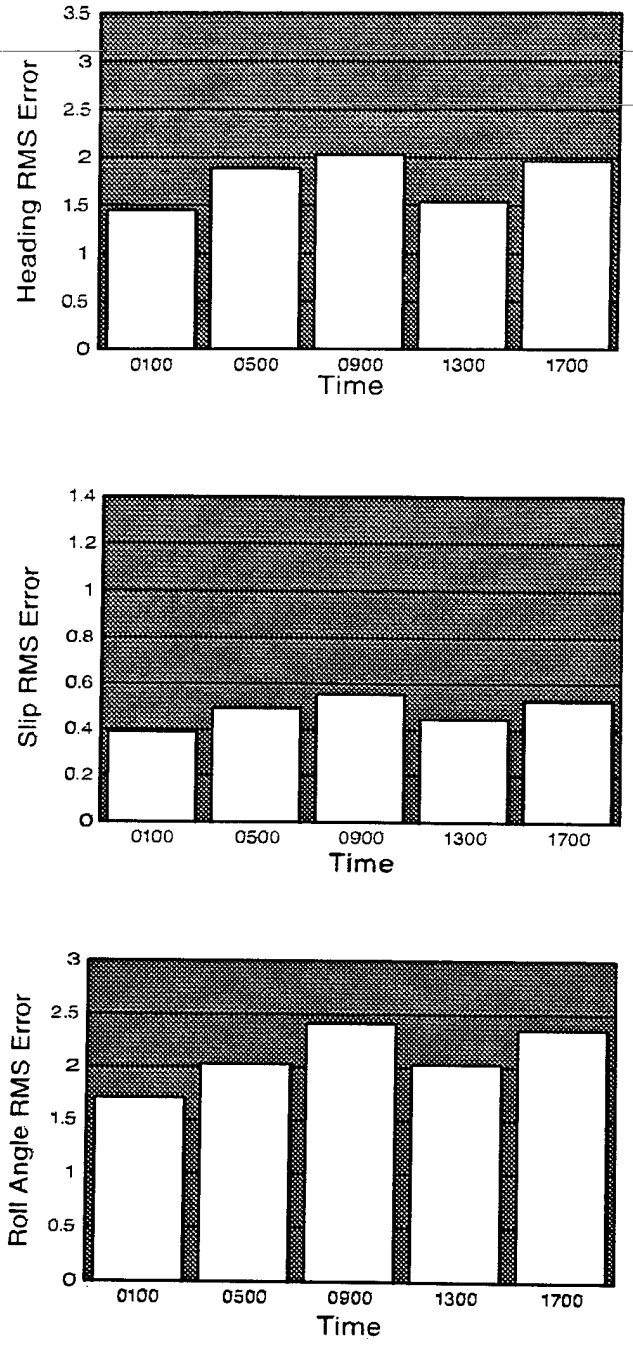


Figure 10. Effects of session on heading, slip, and roll control during the descents.

Electroencephalographic data

The absolute power values from the resting EEGs were analyzed with BMDP 4V repeated measures analysis of variance (Dixon et al., 1990) to determine the effects of drug (placebo, Dexedrine), session (0220, 0620, 1020, 1420, and 1820), and eyes (closed and open). The recording sites that were examined included Fz, Cz, Pz, and Oz. Occasional instances of missing data were handled with BMDP AM which replaced missing values with the means of existing data. After the ANOVAs, significant effects were followed up with appropriate analyses of simple effects and/or contrasts to pinpoint the location of noteworthy differences.

Delta activity

The 3-way ANOVA on absolute delta (1.5-3.0 Hz) power indicated no 3-way interaction, but there was one 2-way interaction between drug and eyes at Cz ($F(1,5)=20.38, p=.0063$). Analysis of simple effects showed this interaction was due to a drug effect at eyes closed ($p=.0173$), but not at eyes open ($p>.05$). During testing with eyes closed, the subjects evidenced significantly more delta under placebo than under Dexedrine, whereas with eyes opened, the amount of delta was equivalent between the two drug conditions.

There were significant main effects on both the drug and the eyes factors. There was more delta activity under placebo than Dexedrine at Fz ($F(1,5)=13.47, p=.0144$), Cz ($F(1,5)=8.54, p=.0329$), and Oz ($F(1,5)=16.00, p=.0103$). These drug effects are depicted in figure 11. In addition, there was more delta under eyes closed than eyes opened at Fz ($F(1,5)=13.99, p=.0134$), Cz ($F(1,5)=12.90, p=.0157$), Pz ($F(1,5)=9.34, p=.0282$), and Oz ($F(1,5)=12.47, p=.0167$). There were not significant differences among the testing sessions at any of the electrodes examined here.

Theta activity

The 3-way ANOVA on absolute theta (3.0-8.0 Hz) power indicated there were no significant interactions at Fz, Cz, Pz, or Oz. However, there was more overall theta activity under placebo than under Dexedrine at Oz ($F(1,5)=17.19, p=.0089$) as can be seen in figure 12. Also, there was more overall theta during eyes closed than during eyes open at every electrode. Main

effects were found on the eyes factor at Fz ($F(1,5)=8.93, p=.0305$), Cz ($F(1,5)=12.13, p=.0176$), Pz ($F(1,5)=11.85, p=.0184$), and Oz ($F(1,5)=10.56, p=.0027$).

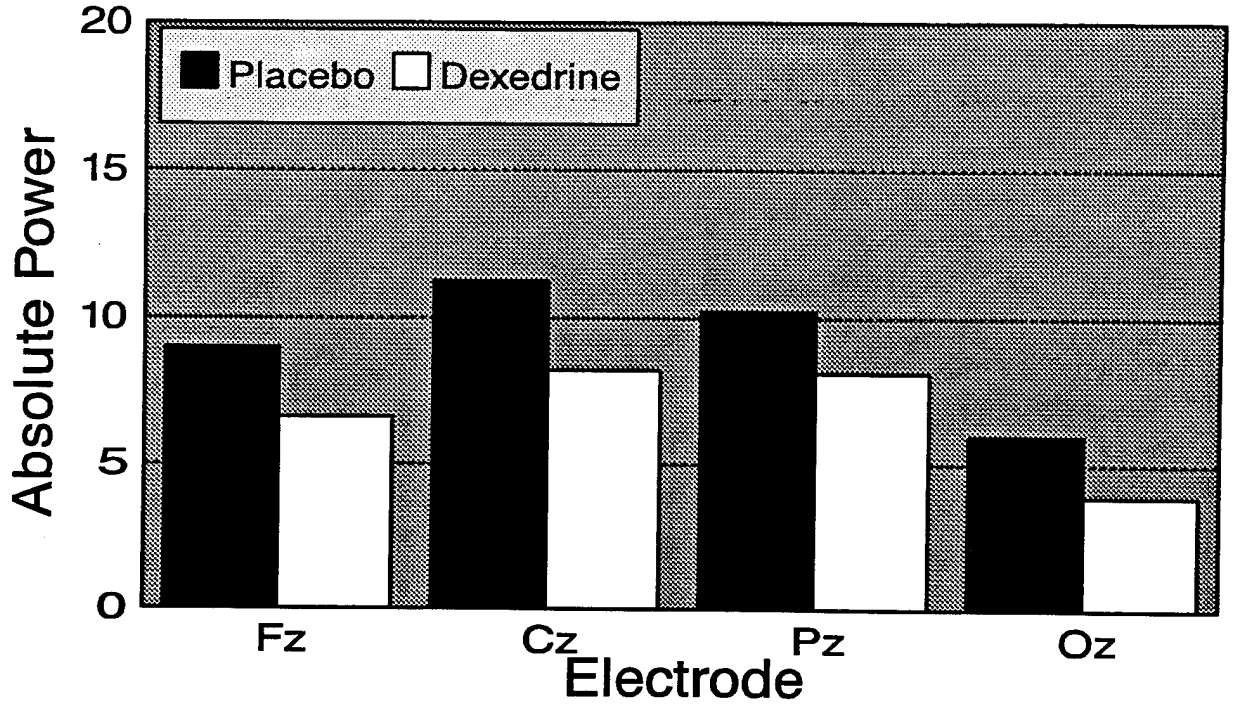


Figure 11. Effects of drug on absolute delta power.

Alpha activity

The ANOVA on absolute alpha (8.0-13.0 Hz) power revealed no 3-way interaction, but there were 2-way interactions between the drug and eyes factors and between the session and eyes factors. The drug-by-eyes interactions were found at Fz ($F(1,5)=7.87, p=.0377$) and Cz ($F(1,5)=7.38, p=.0420$). In both cases, there was a difference between the amount of alpha under placebo versus Dexedrine during eyes closed ($p=.0484$ and $.0496$ respectively), but not during eyes opened ($p>.05$). An examination of the mean alpha power during eyes closed showed more alpha under Dexedrine than under placebo both at Fz and Cz (see figure 13).

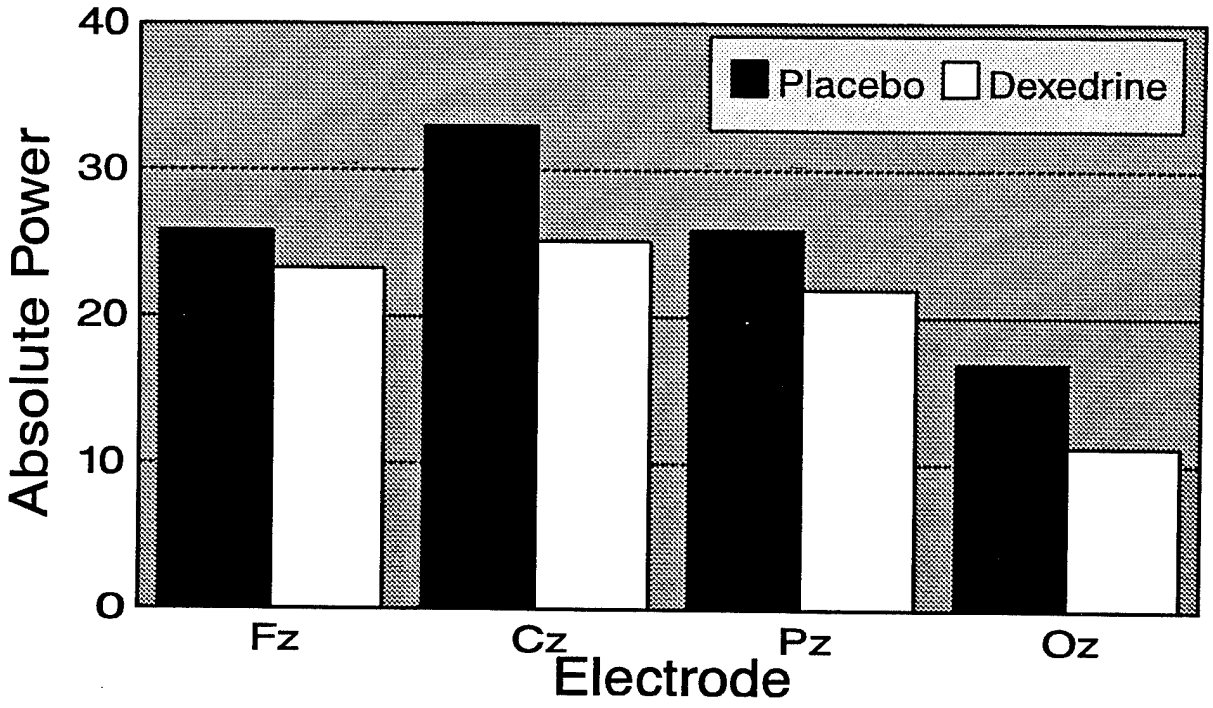


Figure 12. Effects of drug on absolute theta power.

Session-by-eyes interactions were found at Fz ($F(4,20)=3.65, p=.0217$) and Oz ($F(4,20)=3.38, p=.0289$). An examination of the mean alpha power at Fz under eyes closed versus eyes opened showed significant differences at every session throughout the day ($p<.05$) with the exception of the 1420 session. An examination of the alpha activity at Oz, indicated significant differences across all of the sessions, but the mean differences between the eyes-open and eyes-closed conditions were actually larger at 1420 ($p<.0148$) than they were elsewhere.

There were no significant main effects on the drug factor (there was a marginal ($p=.0726$) effect only at Fz), but there were differences between eyes opened and eyes closed at every electrode except Pz. At Fz ($F(1,5)=9.94, p=.0253$), Cz ($F(1,5)=11.12, p=.0207$), and Oz ($F(1,5)=8.35, p=,0342$) more alpha activity was observed during eyes closed than during eyes opened.

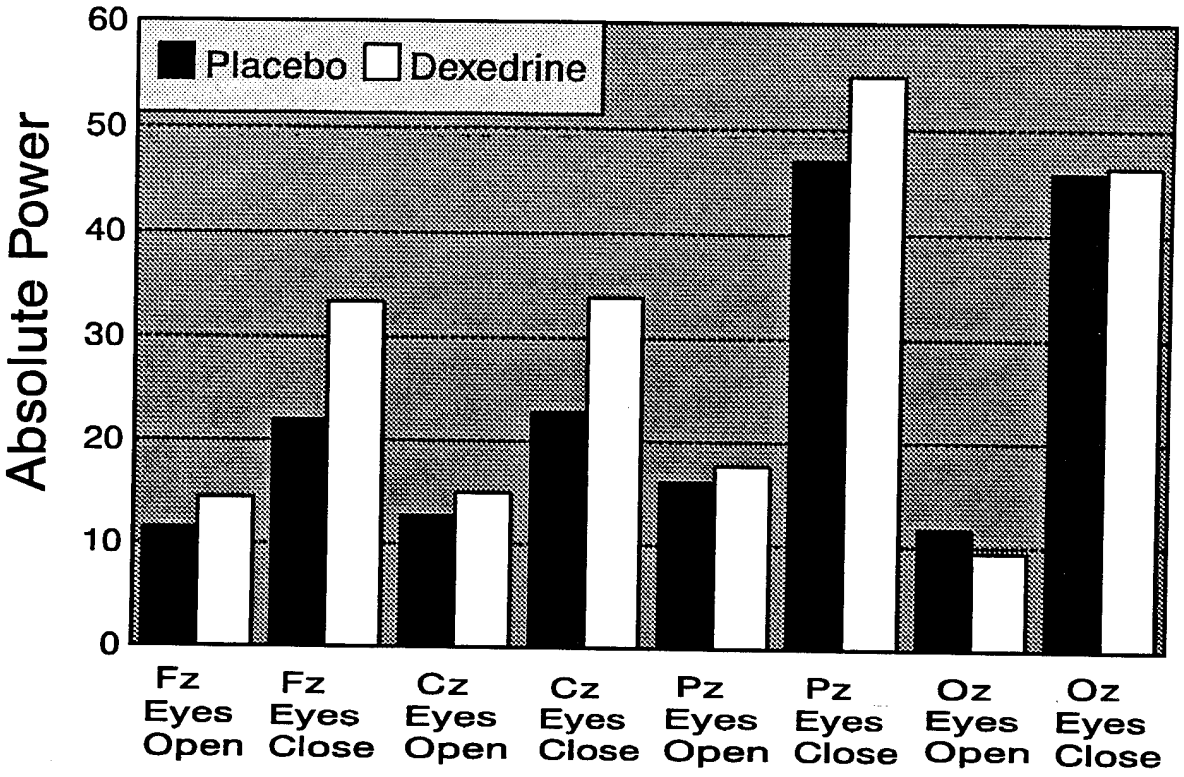


Figure 13. Effects of drug and eye closure on absolute alpha power.

Beta activity

The ANOVA on absolute beta (13.0-20.0 Hz) power revealed no 2- or 3-way interactions. However, there was a main effect attributable to the drug condition at Oz ($F(1,5)=6.99, p=.0457$), and there were main effects attributable to the eyes condition at Fz ($F(1,5)=13.42, p=.0145$), Cz ($F(1,5)=27.22, p=.0034$), Pz ($F(1,5)=15.36, p=.0112$), and Oz ($F(1,5)=9.23, p=.0288$). The drug effect was due to less beta under Dexedrine than under placebo, while all of the eyes effects were due to less beta during eyes open than during eyes closed.

Desktop Flight Simulation Task

Data from the desktop flight simulation task consisted of overall scores, overall reaction times, and reaction times for the low and high turbulence conditions. These data were analyzed with BMDP 4V (Dixon et al., 1990) using the two within-subjects factors of drug (placebo, Dexedrine) and session (0300, 0700, 1100, 1500, and 1900). Significant effects were followed by appropriate posthoc statistics. There were only five subjects who contributed data for this task because some aspects of the task were modified after the first subject completed testing. Among these five subjects, there was a small percentage of missing reaction-time data (one session) from two of the subjects, and these were estimated using means of existing data.

There were no drug-by-session interactions and no drug main effects on any of the four variates examined. However, there were session effects on the overall reaction times ($F(4,16)=4.93, p=.0088$) and the reaction times for the non-turbulent condition ($F(4,16)=4.77, p=.0100$). Contrasts indicated the effect on overall reaction time was due to slower reactions at 0700 than at 0300 and 1500, and slower reactions at 1100 than at 1500 as well ($p<.05$). The effect on reaction time during the non-turbulent condition was a result of reactions being slower at 0700 and 1100 than at 0300 ($p<.05$).

Profile of Mood States

Data from each of the six scales of the POMS were analyzed with BMDP 4V (Dixon et al., 1990). The two within-subjects factors were drug (placebo and Dexedrine) and session (0340, 0740, 1140, 1540, 1940, and 2225). Significant main effects and interactions were followed by appropriate posthoc analyses consisting of simple effects and/or contrasts to pinpoint the location of noteworthy differences.

Tension-anxiety scale

The 2-way analysis of variance on the tension-anxiety scale, which reflects heightened musculoskeletal tension, indicated there was no drug x session interaction and no drug main effect. However, there was a main effect attributable to differences among the six testing sessions ($F(5,25)=5.16, p=.0022$). Contrasts revealed that tension-anxiety scores were lower at 2225 than they were at any of the earlier sessions ($p<.05$) with the exception of

the one at 1940 (there was little difference between the last two testing sessions of the day). In addition, there was a difference between the 1940 scores and those at both 0740 and 1540, where the 1940 scores were the lowest of the three ($p<.05$).

Depression-dejection scale

The ANOVA on the depression-dejection scores indicated there were no drug x session interactions and no drug main effects. There was a session main effect ($F(5,25)=2.61, p=.0496$) apparently due to marginally higher scores at 1140 than at 0340, 1540, 1940, and 2225; however, none of these differences were significant.

Anger-hostility

The ANOVA on the anger-hostility scores, which reflect anger and antipathy towards others, revealed no significant main effects or interactions.

Vigor-activity

The ANOVA on the vigor-activity scale, which reflects vigorousness and high energy, revealed a significant 2-way interaction between drug and session ($F(5,25)=2.55$, $p=.0534$), but there were no main effects due to either drug or session. Analysis of simple effects indicated the interaction was because of increased vigor under Dexedrine in comparison to placebo at 0340, 0740, and 1540 ($p<.05$ for 0340 and 1540; $p=.0586$ for 0740), while there were no differences at the other sessions. These effects are depicted in figure 14.

Fatigue-inertia

The analysis of the fatigue-inertia scale, which reflects a mood of weariness, inertia, and low energy, revealed a significant drug-by-session interaction ($F(5,25)=6.71, p=.0004$) and a significant session main effect ($F(5,25)=2.63, p=.0484$). The interaction was because Dexedrine reduced the fatigue scores in comparison to placebo at 0740 ($p<.05$), but not at the other sessions (see figure 15). The session main effect was due to higher overall fatigue scores at 0740 than at 0340 ($p<.05$). There were no differences among the other sessions.

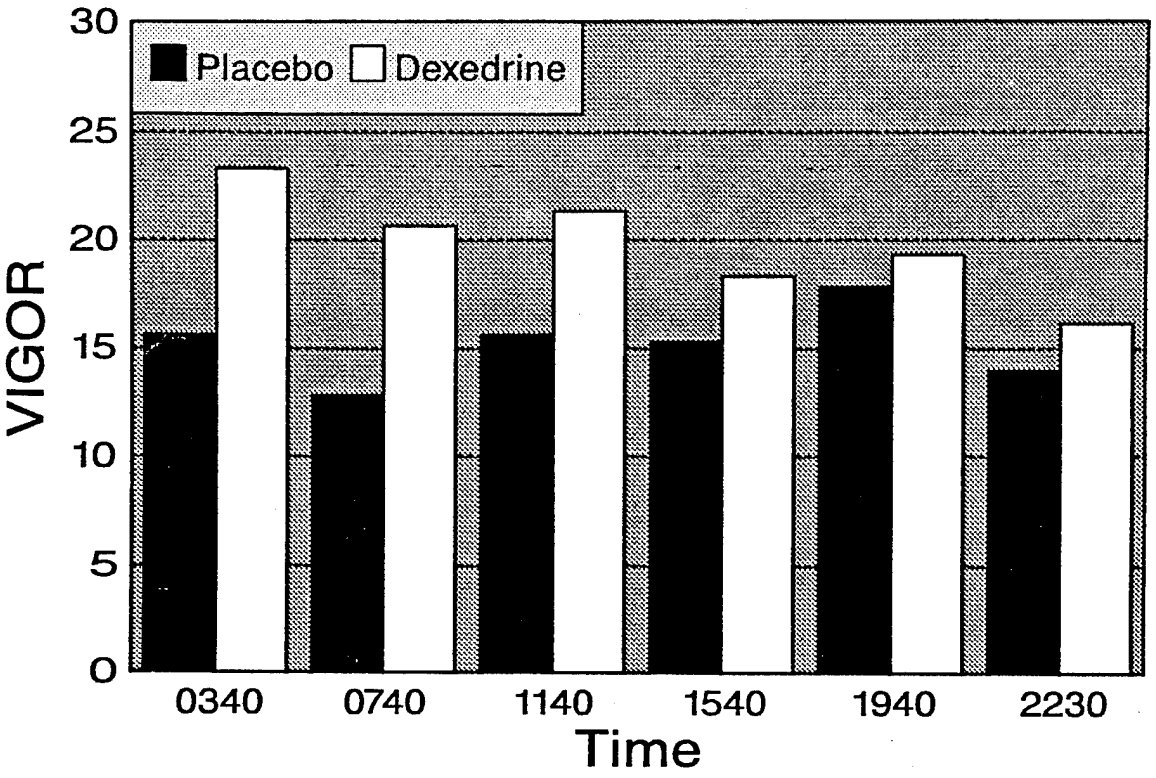


Figure 14. The effect of drug and session on subjective ratings of vigor.

Confusion-bewilderment

The ANOVA on the confusion-bewilderment scale, which reflects bewilderment and muddleheadedness, also indicated a significant interaction between drug and session ($F(5,25)=3.11, p=.0256$), but there were no significant main effects. This was due to a tendency toward greater confusion scores under placebo than under Dexedrine at 0340 and 0740; however, there were no statistically-significant differences at either of these times (the p values were .11 and .07 respectively). The means for each session are shown in figure 16.

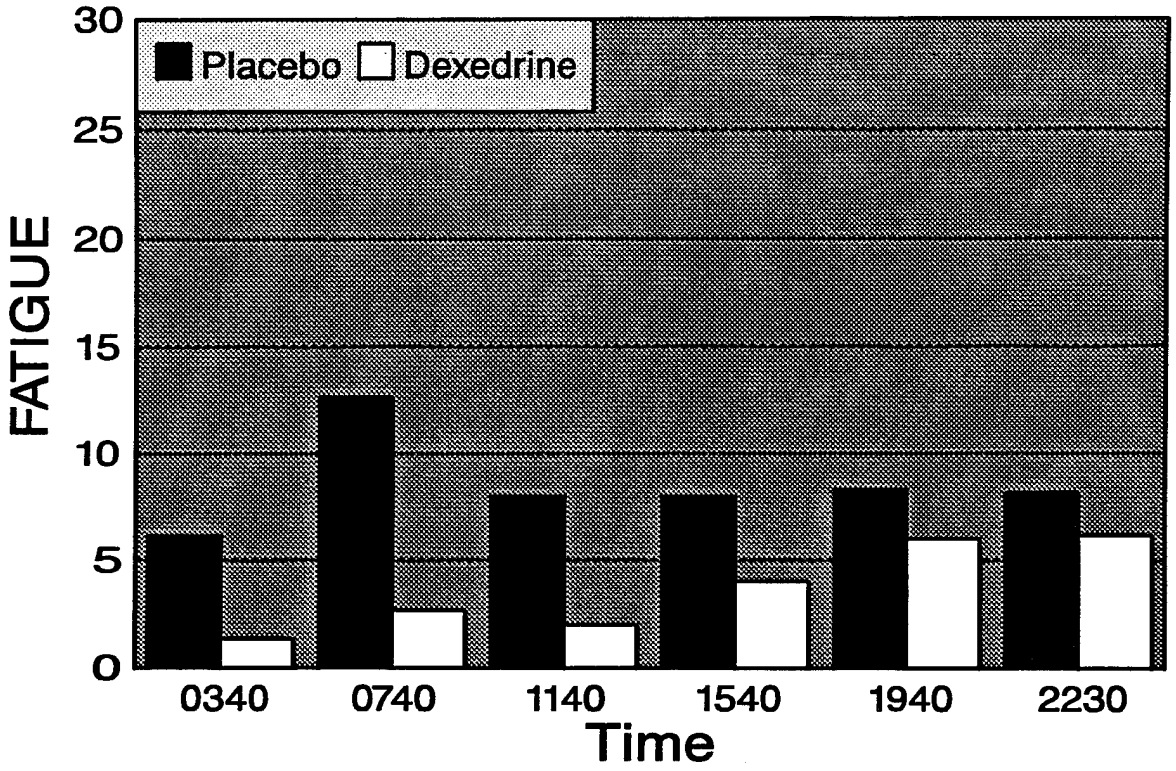


Figure 15. Effect of drug and session on subjective ratings of fatigue.

Synthetic Work Battery

The data from only five subjects were analyzed for this task because computer problems resulted in lost data files for one subject. The data were analyzed with BMDP 4V repeated measures analysis of variance (Dixon et al., 1990) to determine the effects of drug (Dexedrine, placebo) and session (0345, 0745, 1145, 1545, and 1945), as well as interactions between these two factors.

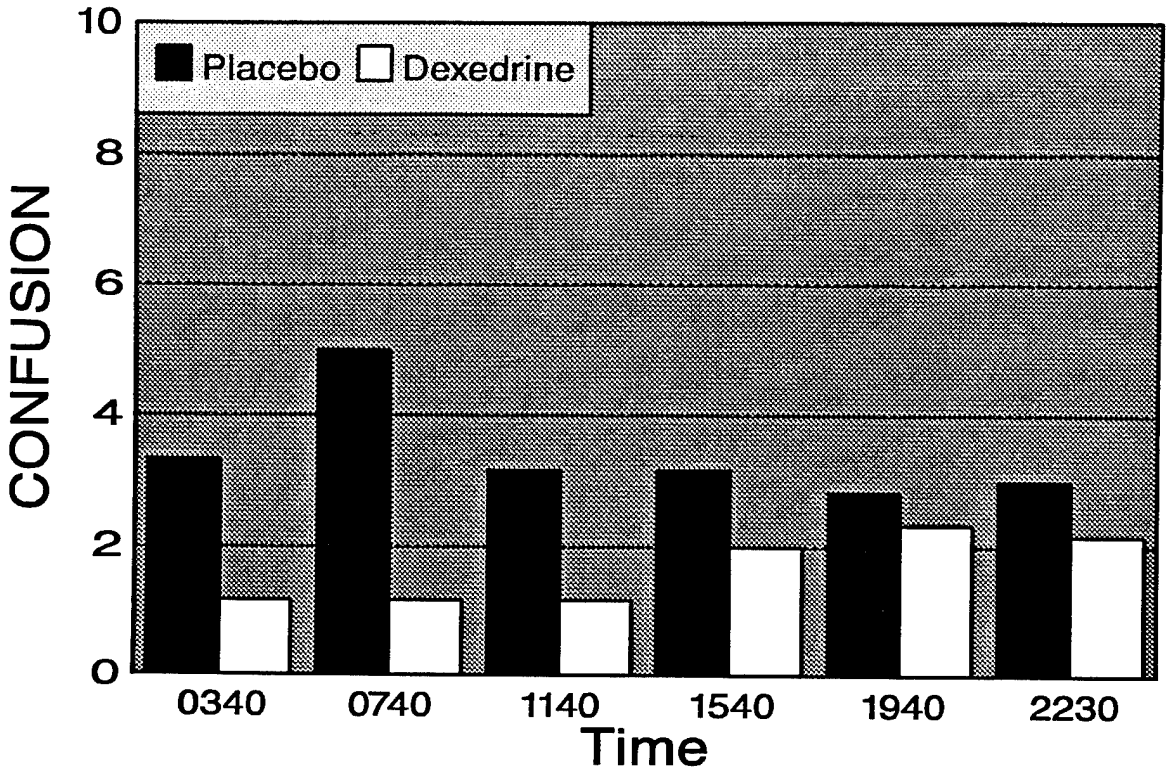


Figure 16. Effect of drug and session on subjective ratings of confusion.

Sternberg task

The percentage of correct responses, the latency to correct responses, and the number of memory-set retrievals were analyzed for this task. The ANOVA indicated there were no significant main effects or interactions on any of these variates.

Arithmetic task

Performance on the arithmetic task was examined in terms of the percentage of correct responses and the amount of time it took to correctly answer problems. The ANOVA indicated there

were no significant main effects or interactions on either variate.

Visual monitoring task

Performance on the visual monitoring task was examined in terms of how far the subjects allowed the pointer to move before resetting it to the center of the computer screen and in terms of how long it took subjects to reset the pointer. Also, the number of times the subjects failed to reset the pointer before it reached the end of the scale was examined. The analysis indicated there were no significant main effects or interactions on any of these variates.

Auditory monitoring task

Performance on this task was evaluated with regard to the percentage of correct responses, the percentage of signals detected, and the detection latency. The ANOVA indicated no significant main effects on any of these variates; however, there was a drug-by-session interaction on the percentage of signals detected ($F(4,16)=3.33, p=.0363$). Analysis of simple effects revealed this interaction apparently was due to a marginal decrease in the signals detected under Dexedrine in comparison to those detected under placebo at 1940 ($p=.0993$); however, none of the simple effects attained significance.

Vital signs data

The vital signs data were collected primarily for safety reasons as opposed to testing any hypothesis. However, these data were analyzed with BMDP 4V repeated measures analysis of variance (Dixon et al., 1990). The two within-subjects factors were drug (Dexedrine and placebo) and time (time 1 through time 24). Only the heart rate and blood pressure data will be reported since many of the temperature readings were confounded by the fact that subjects were eating or drinking in close proximity to the times at which vital signs were collected.

Heart rate

The ANOVA on heart rate data indicated a drug-by-time interaction ($F(22,110)=4.46, p<.0001$), a time main effect

(F(22,110)=3.73,p<.0001), and a drug main effect (F(1,5)=23.53,p=.0047). The time effect will not be pursued further because of the inordinate amount of comparisons which would be necessary to explore this effect and because of its relative lack of importance. However, the drug-by-time interaction was examined with analysis of simple effects. This revealed there were no differences between the Dexedrine and placebo conditions at any time from 0020 through 0450; however, Dexedrine produced a higher pulse rate than placebo at every session from 0610 to 2020 (p<=.05). There was no difference between drug and placebo at 2050 (p=.10), but Dexedrine again was associated with a heart-rate increase at 2220, the last testing time of the day (p<.05). These effects may be seen in figure 17. The overall drug main effect supported the drug-by-time interaction in that Dexedrine produced a higher pulse rate than placebo (83.75 versus 70.90).

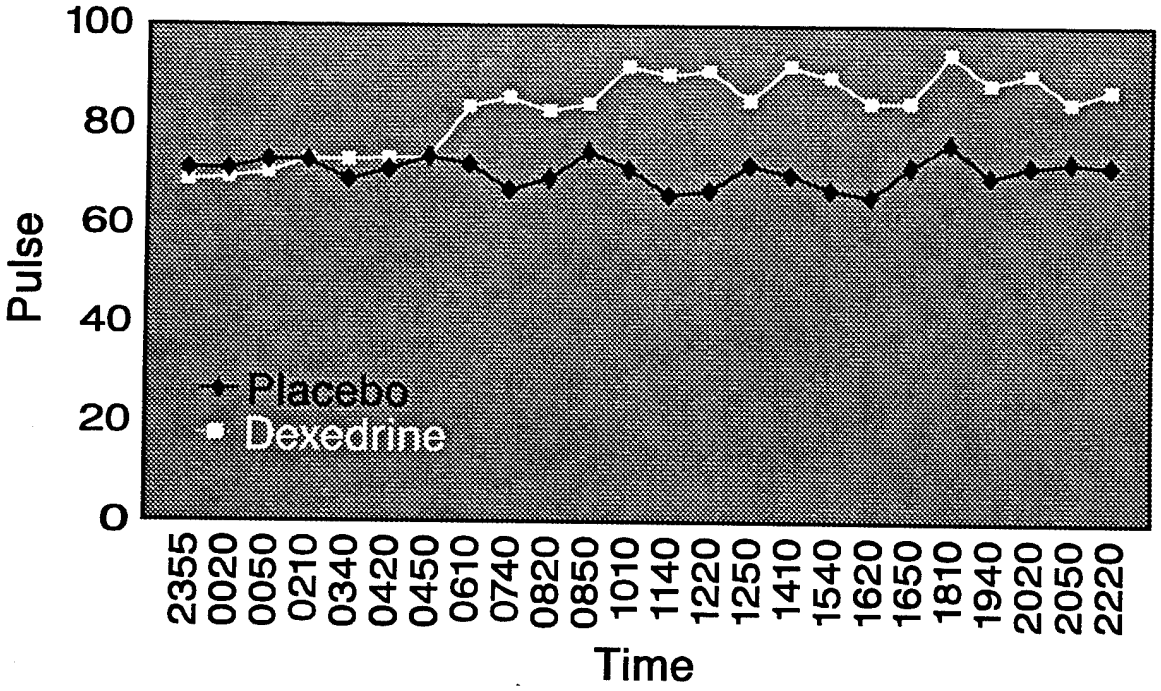


Figure 17. Effect of drug and time on heart rates.

Systolic blood pressure

The ANOVA on systolic blood pressure revealed a drug-by-time interaction (F(22,110)=4.49,p<.0001), a time main effect (F(22,110)=1.99,p=.0107), and a drug main effect

(F(1,5)=14.89,p=.0119). The time effect was not examined further; however, the drug-by-time effect was examined with analysis of simple effects. This showed there were no differences between Dexedrine and placebo from 0020 through 0420, but Dexedrine produced higher systolic pressures at 0450 and at every time from 0850 through 1220 (p,=.05). At 1250, there was a marginally-significant elevation under Dexedrine (p=.06), and the difference again was significant at 1450 (p<.05). From 1540 through 1940, the blood pressures under Dexedrine were equivalent to those under placebo, but there again were Dexedrine-induced elevations at 2020 and 2050 (p<.05) which had dissipated by 2220, the last test of the day (see figure 18). The drug main effect supported the findings from the drug-by-time interaction, indicating that Dexedrine produced an overall elevation in systolic blood pressure in comparison to placebo (127.77 mmHg versus 120.91 mmHg).

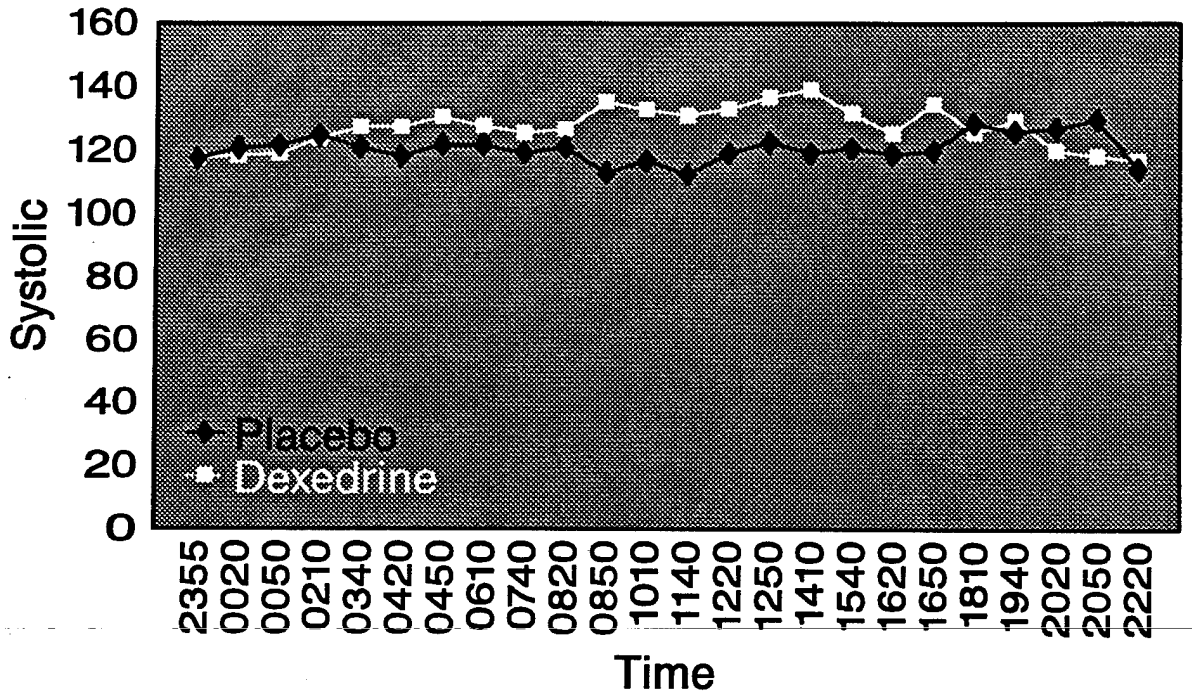


Figure 18. Effect of drug and time on systolic blood pressure.

Diastolic blood pressure

The ANOVA on diastolic blood pressure indicated there was a drug-by-time interaction (F(22,110)=2.27,p=.0028), and a drug

main effect (F(1,5)=35.01,p=.0020). Analysis of simple effects showed the interaction was because there were no differences between Dexedrine and placebo at any of the times between 0020 and 0610, but there were differences later in the day. Specifically, Dexedrine produced higher diastolic blood pressure at 0740, and at every time from 0850 through 1410 (p<=.05). At 1540 and 1620, there were no differences, but later on Dexedrine again was associated with higher diastolic pressures at 1650 and 1940 (p<=.05). The Dexedrine and placebo conditions were equivalent at 1810, 2020, 2050, or 2220 (see figure 19). The drug main effect which depicted the overall impact of Dexedrine versus placebo regardless of time of day revealed that Dexedrine was associated with higher diastolic pressures than placebo (74.81 versus 68.91).

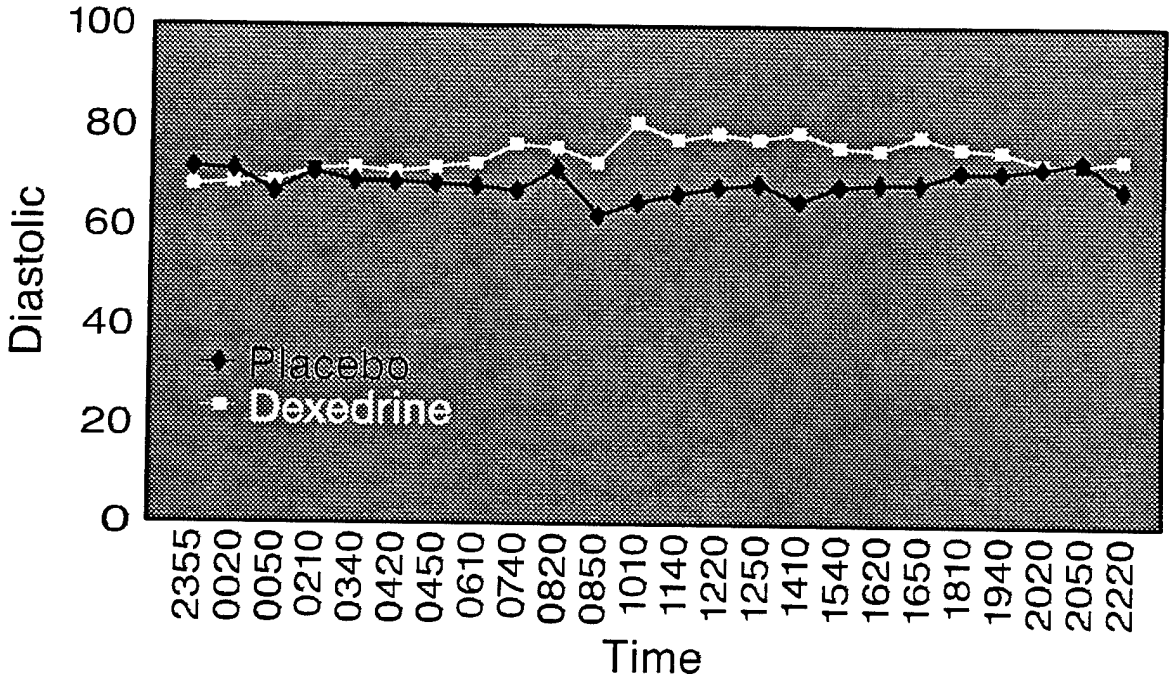


Figure 19. Effect of drug and time on diastolic blood pressure.

Polysomnographic data

Sleep onset (time until the first minute of stage 2 sleep), the percentage of time subjects spent in stages 1-4 and rapid eye

movement (REM) sleep, the percentage of time awake after sleep onset, and the movement time during sleep were analyzed with one-way ANOVAs across three nights (baseline, Dexedrine recovery, and placebo recovery). Prior to the analysis, the percent data were transformed using the 2*arcsin square-root transformation to stabilize the variances (Winer, 1971).

Sleep onset and total sleep

The analyses revealed a significant main effect across the nights on sleep onset ($F(2,10)=4.31$, $p=.0447$). This was due to a faster sleep onset after placebo than during baseline or during recovery sleep after Dexedrine ($p<.05$), but there was no difference between the baseline and Dexedrine nights. The amount of total sleep time also differed across the three nights ($F(2,10)=7.33$, $p=.0110$). Total sleep time during baseline was significantly lower than the amount after Dexedrine and placebo ($p<.05$), with no difference between the two drug recovery nights.

Stages 1-4 sleep

There was a significant main effect due to testing night on the percentage of stage 1 sleep ($F(2,10)=13.02$, $p=.0016$). Subsequent contrasts indicated this was due to a decrease in the percentage of stage 1 sleep after placebo in comparison to Dexedrine and baseline ($p<.05$), but there was no difference between baseline sleep and the sleep after Dexedrine. There also was a significant change in the percentage of stage 2 sleep ($F(2,10)=4.32$, $p=.0445$), which was due to a decrease in stage 2 following placebo in comparison to the amount of stage 2 during baseline sleep with no difference between baseline and Dexedrine. There was a tendency for percent stage 2 sleep to be lower following placebo than following Dexedrine ($p=.08$), but this was not significant. No differences among the three nights occurred for percent stage 3 sleep, but there was a significant change in stage 4 sleep ($F(2,10)=9.24$, $p=.0053$). This was because of an increase in the percentage of stage 4 sleep following both placebo and Dexedrine in comparison to the amount of stage 4 during baseline.

REM sleep

The percentage of REM sleep also was affected by testing condition ($F(2,10)=14.38$, $p=.0011$). There was a significant

increase in REM following placebo when compared to baseline sleep and sleep following Dexedrine ($p<.05$), but no differences occurred between the baseline night and recovery night following Dexedrine.

Awake and movement time

Although there was a significant difference in the amount of time awake after sleep onset ($F(2,10)=7.33, p=.011$), contrasts did not reveal any significant differences among the 3 nights. There was no significant differences among the 3 nights in the amount of movement time. (See figure 20).

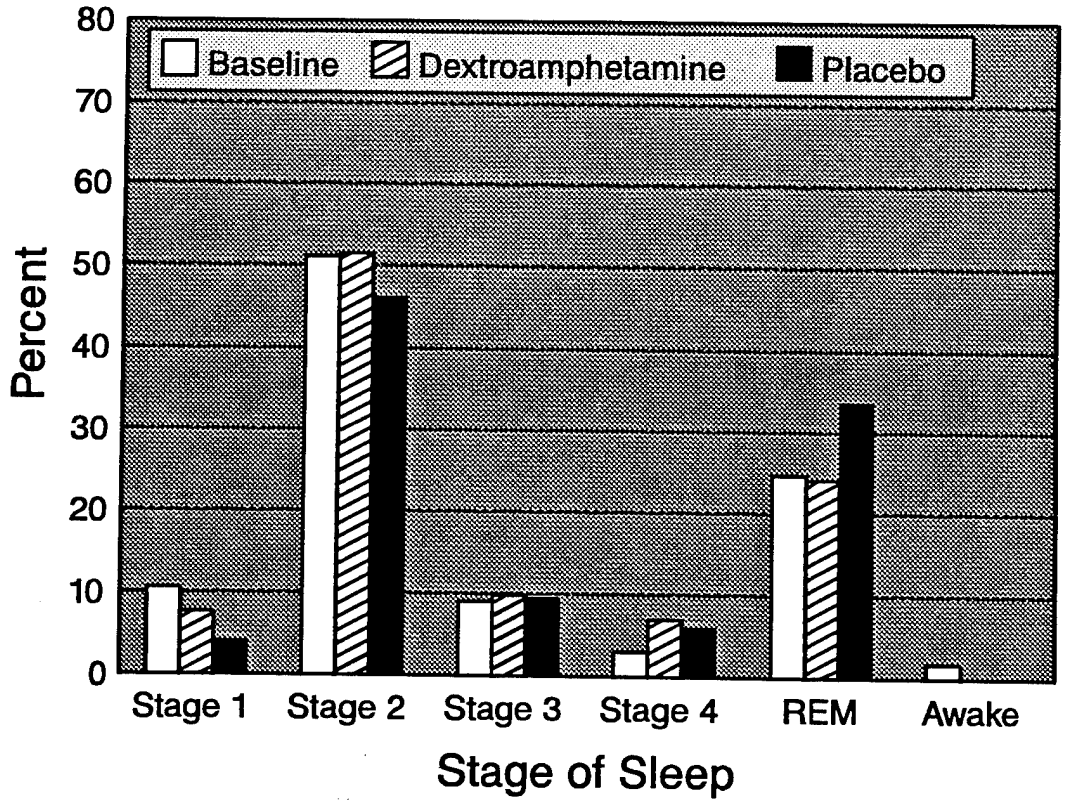


Figure 20. Effect of drug on recovery-sleep stages.

Discussion

Flight peformance

At least one aspect of flight performance (heading, altitude, airspeed, etc.) improved under Dexedrine in comparison to placebo on every maneuver with the exception of the hovers. There were overall drug main effects on the low-level navigation, straight-and-levels, right standard-rate turns, climbs, descents, and the left descending turn. There also were drug-by-session interactions on several of these maneuvers with the addition of the left standard-rate turns. In virtually every case where there were drug-related effects, performance was better under Dexedrine than it was under placebo. Considering both drug main effects and interactions, this was the case for altitude control during the straight and levels, the left and right standard-rate turns, and the low-level navigation; airspeed control during the right standard-rate turn and the climb; heading control during the descent, the climb, and the low-level navigation; roll control during the descent; slip control during the descent and the left-descending turn; and vertical speed control during the climb, the descent, and the left-descending turn. The single exception to the Dexedrine-better-than-placebo finding occurred in a 3-way interaction among drug, session, and straight-and-level iteration. Here, altitude control in the third straight and level was better under placebo than under Dexedrine at 0100 and 1700 (but control under Dexedrine was better in comparison to placebo at 0900 both for the third and fourth iterations).

The 2-way interactions between drug and session on 5 of the maneuvers showed that out of 14 significant differences between Dexedrine and placebo, only one each was found at 0100 and 1700; and two each were found at 0500 and 1300. The eight remaining differences were observed at the 0900 flight. In every case, regardless of time of day, performance was better under Dexedrine than under placebo.

These findings are consistent with what was expected based on interactions between the amount of sleep deprivation, the timing of the circadian cycle, and the half-life of Dexedrine. At the earliest session of the day, subjects were not suffering from significant sleep deprivation since this was only 2 hours past their normal bed times. Thus, Dexedrine's effects were not evident because performance under placebo had not begun to deteriorate at this point. However, by 0500 both alertness and peformance were beginning to decline due to sleep loss and

fatigue under the placebo condition, and by 0900 the subjects who had not received Dexedrine were having substantial difficulty remaining awake. As the day progressed, subjects recovered somewhat due to circadian effects which tended to improve alertness during normal daylight hours. In fact, most subjects reported "getting their second wind" around noon on their sleep deprivation days (under placebo). By 1700, performance under the two drug conditions was equivalent possibly because circadian effects were improving the situation under placebo while the amount of time from the last dose (9 hours) was degrading performance under Dexedrine.

Overall, it appears that Dexedrine was useful for the sustainment of female helicopter pilot performance during the simulated periods of sustained or continuous operations studied here. These findings are in general agreement with the findings from a similar investigation which was conducted earlier using male subjects (Caldwell, Caldwell, Crowley, and Jones, in press) and previously published anecdotal reports (Cornum, 1994; Senecal, 1988).

Electroencephalographic activity

The analysis of EEG data from the midline electrodes showed that both delta (1.5-3.0 Hz) and theta (3.0-8.0 Hz) activity were greater under placebo than under Dexedrine (an indication of reduced alertness under placebo). The effect on delta activity was fairly widespread. Drug-related differences in this 1.5-3.0 Hz activity were detected at Fz, Cz, and Oz. The effect on theta was less pronounced (significant only at Oz). The amount of alpha activity (8.0-13.0 Hz) also was affected by whether subjects received placebo or Dexedrine, but the drug effects were noticeable only under the resting eyes-closed condition. At both Fz and Cz, mean alpha power was greater under Dexedrine than placebo during the eyes-closed condition. Beta activity (13.0-20.0 Hz) was affected by the drug condition only at Oz where there was a decrease under Dexedrine in comparison to placebo.

There were no drug-by-session interactions on either slow or fast EEG activity because the drug and placebo effects apparently remained relatively constant throughout the day. This was probably because CNS alertness already had degraded under placebo by the time of the first test session (0220) whereas CNS alertness under Dexedrine already was being maintained at this same time. If there had been an EEG session very early in the sleep deprivation period (prior to 0100), this probably would

have produced a drug-by-session effect since there would not have been differences attributable to the drug condition early in the night, but there would have been drug-related effects later.

Overall, the EEG data indicate that central nervous system (CNS) arousal was impacted adversely by sleep deprivation under the placebo condition while Dexedrine mitigated this effect. The presence of elevated slow-wave EEG activity under the placebo condition is consistent with the findings of other investigations on the effects of sleep deprivation (i.e., Pigeau, Heslegrave, and Angus, 1987). The fact that alpha activity was affected only under the eyes-closed condition probably reflects the fact that subjects were tending to fall asleep (under the placebo condition) when they were required to sit quietly, even for a few seconds, with their eyes closed. The attenuation of alpha activity is an indication of the onset of sleep.

The EEG differences under Dexedrine versus placebo are consistent with the overall findings from the flight performance data. Although EEGs were not recorded during the simulator flights, they were collected about 30 minutes after each flight. Thus, it is reasonable to utilize the overall findings of reduced CNS alertness under placebo versus Dexedrine to explain degraded performance under the placebo condition. It is noteworthy that Dexedrine maintained both flight performance and CNS alertness throughout the deprivation period.

Desktop flight simulation task

The results from the flight simulation task showed that there were no significant drug effects on the overall performance scores (time and accuracy of flying) or on the reaction time data (from the secondary auditory task). These results differ from the results of a previous study (Caldwell et al., 1994) in which it was found that male pilots did show decrements on this task across the testing sessions under placebo, but not under Dexedrine. Reasons for this discrepancy are not readily apparent now, but subjective observations did suggest that it was more difficult for the experimenters to guess whether the females were receiving drug or placebo than it was to guess the drug/placebo conditions for the males. Perhaps this group of female subjects simply tended to be less affected by sleep deprivation in general than our earlier sample, and thus, the differences between Dexedrine and placebo were not as pronounced.

Profile of mood states

The data from the POMS showed that the subjects' subjective feelings of tension-anxiety, depression-dejection, and anger-hostility were not affected by whether they received Dexedrine or placebo. However, there was less overall tension toward the end of the deprivation period than at the beginning.

There were drug-by-session interactions on vigor-activity, fatigue-inertia, and confusion-bewilderment. At 0340 (and marginally at 0740) subjects' feelings of vigor were improved by Dexedrine in comparison to placebo. A similar effect also occurred as late as 1540. The subjects' feelings of fatigue were reduced greatly by Dexedrine versus placebo at 0740, and feelings of confusion tended to be reduced by Dexedrine at 0340 and 0740. These results tend to support those of Newhouse et al.(1989) who found that dextroamphetamine (relative to placebo) improved vigor and fatigue ratings following a period of sleep deprivation.

The fact that the majority of drug-related differences were evident early in the deprivation period is consistent with the earlier interpretations of the flight performance data. Subjects were experiencing the most difficulty maintaining alertness under the placebo condition at the time nearest to the 0900 flight where the greatest differences between Dexedrine and placebo were found. The differences in confusion-bewilderment scores also seem to indicate that subjects may have had problems thinking clearly during the 0500 and 0900 flights.

Synthetic work battery

Cognitive performance as measured by the synthetic work battery was not substantially affected by either the drug condition or the testing session. There were no significant effects on the Sternberg memory task, the arithmetic task, or the visual monitoring task. However, there was a difference between Dexedrine and placebo (a drug-by-session interaction) on one measure of auditory monitoring. On this task, subjects tended to correctly detect more tones under placebo than Dexedrine at the last session of the day, but not at other times; however, this effect was not statistically significant. The reasons why this reversal of placebo/Dexedrine effects tended to occur at the last session of the deprivation period is unclear. Perhaps the difference was due to motivational factors. The sleep deprived subjects who were under the placebo condition may have been able to improve on their earlier performance when they realized they

would soon be finished with the testing day, whereas the Dexedrine subjects might have been performing more poorly because they felt the drug effects wearing off.

Overall, the lack of sleep-deprivation effects and the drug/placebo reversal on the synthetic work battery appears inconsistent with the UH-60 simulator, EEG, and POMS data. However, as was noted previously (Caldwell et al., 1994), it may be that longer testing sessions (i.e., greater than 10 minutes) are required to detect fatigue-induced problems on certain types of cognitive performance. Subjects appear to enjoy performing the synthetic work battery, and thus, it is possible that the brief requirement to complete this interesting task may have had an alerting effect which was not counteracted by vigilance problems (because the task was so short). In the future, a task duration of approximately 30 minutes probably would offer greater insight into the cognitive decrements associated with sleep loss.

Vital signs

The subjects' vital signs were significantly elevated by Dexedrine, and there were clear interactions between the magnitude of drug effects and the time at which the vital signs were collected. Heart rate was not different under Dexedrine versus placebo until after 0450. Then, starting at 0610 (the next collection time), Dexedrine produced elevations in heart rate which persisted until late in the day (until 2020). Systolic blood pressure was unaffected similarly by the drug conditions early in the morning. However, after 0420, systolic pressure increased under Dexedrine and remained elevated for most of the day until 1540, at which time the differences disappeared (with the exception of a brief recurrence at 2020 and 2050). Diastolic blood pressure was unaffected by Dexedrine until after 0850 at which time pressure was elevated until 1410. Afterwards, diastolic blood pressure was unaffected by Dexedrine for most of the remainder of the day (with the exception of 1650 and 1940).

Although oral temperatures were not statistically analyzed due to the fact that they were occasionally confounded by the subjects' consumption of cold drinks and hot food, these data were collected for safety monitoring purposes. It should be noted that one subject experienced significantly elevated oral temperature on her Dexedrine-administration day (99.9 degrees Fahrenheit), and this was accompanied by increased heart-rate (131 beats per minute) and elevated blood pressure (153/76 mmHg). Such changes were interpreted as an idiosyncratic response to

Dexedrine which was not significant in clinical terms (the subject was in no danger and did not complain of any discomfort). However, this subject did have the lowest body weight of the sample (112 pounds) which raises the possibility that these effects could have been associated with the elevated amount of drug per unit of weight in this participant. All vital signs were within normal limits by the end of the deprivation day.

Polysomnography

The overall sleep quality of subjects tended to be better during both of the recovery nights following sleep deprivation than it was on the baseline night as evidenced by faster sleep onsets, increased consecutive minutes asleep, and elevated amounts of stage 4 sleep. However, sleep quality on the placebo recovery night appeared to be the best of all 3 nights in terms of decreases in stages 1 and 2 sleep, and increases in REM sleep.

These data suggest that even though subjects still had a substantial amount of amphetamine in their systems on the Dexedrine recovery night, the pressure to sleep from sleep deprivation was sufficient to allow relatively restorative sleep. Two of the six subjects did complain about their sleep quality following Dexedrine administration, but the remaining four subjects did not voice similar concerns. Of course, the ultimate test of whether recovery sleep following Dexedrine was actually as restful as the sleep following placebo will require analyses of next-day performance. Although there were too few subjects in the present sample to perform statistically meaningful drug comparisons on this single recovery day (three subjects per group), a future effort will address this issue. Previously tested males will be combined with the females studied here to yield an adequate sample size, the next-day performance effects will be analyzed, and the results will be reported elsewhere.

Conclusions

This study was the first placebo-controlled, systematic investigation of the use of Dexedrine to maintain female helicopter pilot performance during moderate sleep deprivation. The study was designed to systematically replicate an earlier study which was performed on male subjects. The results indicated that Dexedrine generally was effective for sustaining flight performance, alertness, vigor, and clear thinking in

comparison to placebo. These positive effects were obtained without behavioral or physiological complications; although there were overall elevations in both pulse and blood pressure, and one subject did experience nonclinically-significant elevations in vital signs after the full dose of Dexedrine.

These data support earlier suggestions that dextroamphetamine administration should be considered a viable alternative for sustaining the alertness and performance of aviation personnel during sustained and/or continuous operations (Senechal, 1988; Cornum, 1994; Emonson and Vanderbeek, 1995; Caldwell, Caldwell, Crowley, and Jones, in press). Dexedrine appears to work well when administered prophylactically in order to prevent the decrements which normally are expected after sleep deprivation.

Qualitative comparisons between the female subjects from this study and the male subjects from a previous investigation suggest that while both groups of subjects experienced significant benefit from Dexedrine, the females probably did not derive as much benefit as did the males. A quantitative study to statistically determine the exact extent of such differences is underway. However, it is not anticipated that operationally-significant gender differences will be observed.

In light of the present data, it is clear that sleep-deprived males and females displayed significantly fewer performance and alertness problems when administered Dexedrine in comparison to placebo. Therefore, Dexedrine should be considered an effective countermeasure for the short-term alleviation of fatigue-induced degradations in sustained operations.

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